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GASTRO-ŒSOPHAGEAL REFLUX IN INFANCY AND CHILDHOOD.[1]

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UNTIL the last decade the phenomenon of gastro-œsophageal reflux—that is, the flow of gastric contents back into the œsophagus—was practically unknown. Clinical interest at that time was directed chiefly to the diagnosis of œsophageal strictures in children, which were all regarded then as congenital strictures. In 1931, Findlay and Kelly pointed out that most children with strictures of the lower half of the œsophagus had stomach within the thorax, interposed between the stricture and the diaphragm. They postulated that these strictures were therefore secondary to a congenital defect, one of intrathoracic stomach with congenital shortening of the œsophagus. They held that these strictures would respond to dilatation, but nothing could be done to relieve the congenital shortening of the œsophagus. During the 1940's P. R. Allison and A. S. Johnston published a series of studies of œsophageal strictures and hiatal herniæ in adults. They stressed the importance of gastric reflux in all these cases in the production of reflux œsophagitis, which in turn they held responsible for the production of fibrosis of the muscle coats of the lower part of the œsophagus. This resulted in stricture formation if the circular fibres were contracted, and shortening of the œsophagus with traction of the stomach into the thorax if the longitudinal coat was involved.

In the pædiatric field it was then realized that some children with intrathoracic stomach had a condition similar, clinically and radiologically, to the adult condition described by Allison. There were now two main schools of thought about intrathoracic stomach in childhood. The first held that the primary defect was congenital shortening of the œsophagus and therefore could not be directly relieved. The second postulated that the primary defect was in the hiatus of the diaphragm, which could be repaired after mobilization of the œsophagus to prevent subsequent inflammatory shortening or stricture. This latter conception gave impetus to the earlier diagnosis of hiatus hernia and intrathoracic stomach in infancy and childhood. On the Continent, particularly in Paris and Scandinavia, there was a wave of surgical enthusiasm for treating intrathoracic stomach as early as possible in infancy in order to prevent stricture formation. Duhamel operated on 31 children with hiatus hernia in a series of 67 cases diagnosed. Seventeen of the children were operated on before twelve months of age, and one as early as two weeks of age. Duhamel was able to mobilize and lengthen the œsophagus in all 31 cases. In young children demonstration of a short œsophagus which cannot be lengthened is an increasingly rare phenomenon.

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 13 to 16, 1956.

It is obvious that with increasing interest and investigation more frequent and earlier diagnosis could be made, and a much wider field of clinical material offered itself for study of the course and relationships of these conditions. As more uncomplicated herniæ were revealed the question arose what proportion would progress to form larger herniæ or strictures. What happened in those cases in which complications did not occur? These questions must be answered before proper appraisal of surgical or medical results can be made.

Medical progress has been slower and the surgical approach was justified by the negative attitude of most physicians in this field of clinical observation. Little discussion or interest was shown in the detailed medical management of these children, who were usually transferred to otolaryngologists for dilatation or to surgeons for emergency gastrostomy. Allison and Johnston in their studies have given more than a technique of hiatal repair: they have made considerable progress in pathological studies and have stressed the importance of posture and of an ulcer regime in the medical approach to treatment of reflux and œsophagitis, particularly in the early uncomplicated stages.

In 1946, Wyllie and Field described in a small group of six children a clinical syndrome which they called gastro-œsophagitis. They pointed out that this syndrome, characterized by vomiting, blood in vomitus or stools, and some degree of anæmia or failure to thrive, was common to a variety of conditions ranging from simple gastric reflux to hiatus hernia with ulceration, or congenital shortening of the œsophagus with intrathoracic stomach.

In 1947, Neuhauser described an apparently new syndrome in young infants, called simple relaxed cardia of unknown ætiology, characterized by vomiting commencing very early in life, and by constant gastric reflux with an open hiatus on radiological examination. As the first few children with this type all recovered clinically within a period of months or a year or two, the relation of this simple syndrome to children with hiatus hernia was not immediately apparent, despite the clinical similarity pointed out by Wyllie and Field. It was soon evident on the examination of vomiting babies that both these groups had not only the same clinical picture, but the same basic physiological disorder, namely, gastric reflux; they differed, however, in the radiological outlines observed. Further intermediate cases were seen in which features of both types were present — that is, hiatus hernia and simple relaxed cardia—at different times or even at the one examination.

In December, 1952, Carré, Astley and Smellie made an important contribution with their analysis of 112 children with minor intrathoracic stomach. These children were followed for varying periods with simple medical measures, and the vast majority, over 90%, ran a benign course with complete clinical recovery, occurring rapidly in some instances and more slowly in others. In only one case was the condition actually observed to reach the stage of stricture formation. This was the first large series of cases to be published with a critical analysis of the degree of severity of the clinical picture of hiatus hernia, and of its course and prognosis in infancy and childhood.

Because of its relation to hiatal hernia the radiological assessment of gastric reflux has now become a well-established part of radiological investigation of vomiting children. New problems have arisen in considering the causes and effects of reflux and their application to clinical study. A brief review of the usual conditions found in the examination of the swallowing functions of young, normal children will bring into better focus the various degrees of clinical disorders about to be described.

Radiological Appearances of the Œsophagus in a Normal Infant.

While an infant swallows fluid, as in sucking from a feeding bottle, the œsophagus appears as an evenly distended column with a constant narrowing like a pencil-point at hiatus level before opening tangentially into the rounded stomach fundus (Figure I). If the child is old enough and if it can be induced to swallow a large bolus of thick barium cream, a wave of distension is revealed followed by a wave of peristalsis along the length of the œsophagus. With a firm bolus the hiatus may share this wave of distension, but will contract again immediately after the bolus has passed (see Figure I). More often when the bolus is softer in consistency it is held up in the region of the ampulla and then slowly dribbles through the constantly narrowed hiatal canal. During barium examination it is essential to feed the baby as normally and comfortably as possible. Faulty feeding technique with hungry gulping or excessive air swallowing, resulting

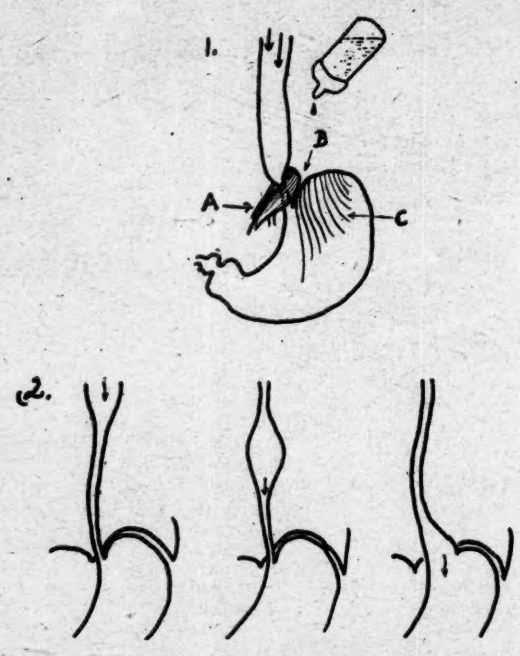

FIGURE I.

1. While the patient is swallowing fluid the pencil-point hiatal canal is seen. (*a*) Hiatal sling. (*b*) Œsophago-gastric angle. (*c*) Inner oblique muscle fibres. 2. Progress of bolus to show distensibility of the hiatus, as in the passage of a small coin or foreign body.

from an unsuitable teat, may cause vomiting or sporadic reflux in a normal child. Only if reflux is maintained for several seconds at least and repeated under reasonably comfortable conditions is it regarded as significant. Further detailed studies of normal swallowing and of eliciting reflux have been described by Astley (1954) and Plarre (1953).

The mechanism for preventing reflux is served partly by the diaphragmatic crura and in part by the structures of the œsophago-gastric junction. The hiatal sling of the right crus of the diaphragm has been described as the extrinsic mechanism, but the intrinsic mechanism is probably more important under normal conditions. Three factors control the intrinsic mechanism: (*a*) The angular entry of the œsophagus into the side of the dome of the fundus. As the dome of the fundus fills with air or fluid, it rises and presses against the hiatal canal (see Figure I (1)). (*b*) The inner oblique fibres of the stomach forming a *s*-shaped sling which pulls down and accentuates this angle when contracted. (*c*) The star-shaped mucosal valve mechanism, which is represented schematically in Figure II. Dornhorst and his co-workers have shown the importance of an intrinsic mechanism in their balloon pressure studies and have postulated a mucosal valve as the medium of this function. For many years the presence of an intrinsic mechanism was attributed to an internal

muscular sphincter at the cardia which could never be demonstrated anatomically, but which was associated with the thickening of the circular muscle occurring in cardiospasm.

Anatomically, the normal mucous membrane of both stomach and œsophagus is very mobile, owing to the thickness of the submucosal coat, and a star-shaped valve is formed by the pulling up of a ring of thicker mucosal folds of the stomach into the hiatal canal, which is already narrowed by the oblique gastric fibres and crura. This pull is made by the *muscularis mucosæ* of the lower part of the œsophagus; the *muscularis mucosæ* is particularly

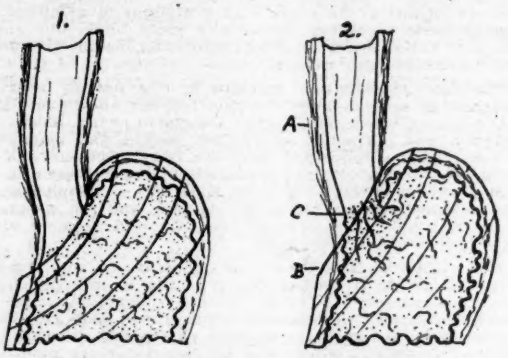

FIGURE II.

Mucosa of gastro-œsophageal junction. 1. Relaxed. 2. Competent cardia. (*a*) Longitudinal *muscularis mucosæ*. (*b*) Inner oblique muscle fibres pulling down the œsophago-gastric angle. (*c*) Puckering of gastric mucosa at the hiatus.

well developed in this part of the œsophagus and its fibres are arranged chiefly longitudinally — an admirable anatomical adaptation for producing the star-shaped mucosal puckering of the competent cardia. Creamer (1955) has postulated that hyperæmia and swelling of the mucosa, as in gastritis or neoplastic infiltration or even normal post-prandial hyperæmia, may result in turgidity and lack of mobility of the mucosa, which in turn will interfere with its valvular efficiency, thus allowing reflux to occur.

The clinical picture of infants and young children with well-established reflux is characteristic and has been described by various authors, including Carré, Astley and Smellie, and Wyllie and Field. Briefly it consists of vomiting, which usually commences in the first week or two of life, the vomitus being commonly blood-stained or having a coffee-grounds appearance, together with some degree of anæmia or failure to thrive. Dysphagia may occur, though this does not always indicate the presence of a stricture. On fluoroscopic examination these patients are seen to have gastric reflux together with a variety of radiological appearances which are represented schematically in Figure III.

Number (i) in Figure III is normal for comparison, showing the even calibre of the fluid-filled œsophagus with pencil-point passage to the stomach, and the star-shaped puckering of the mucosa at the cardia without reflux. Number (ii) is a simple cardio-œsophageal relaxation with constant gastric reflux, an open hiatus with loss of the œsophago-gastric angle, and some widening and atonia of the œsophageal wall. Number (iii) has a small button of obvious gastric folds above the diaphragm and apparent shortening of the œsophagus—corresponding to the type called "minor intrathoracic stomach". Sometimes this gastric pouch may be observed to slip up and down so that the appearances are like numbers (ii) and (iii) combined. Number (iv) has a larger hernia with more shortening of the œsophagus and apparent short stenosis. Number (v) has a longer type of stricture frequently associated with a more tent-shaped stomach above the diaphragm, which is often very difficult to fill out and demonstrate adequately with barium.

Case Histories.

Case I.

An example of simple cardio-œsophageal relaxation is seen in Figure IV. The patient, J., was only ten days old and had had symptoms of projectile vomiting of blood-stained vomitus for one week. The plate depicts the radiological findings of constant reflux with an open hiatus and widening of the lower end of the œsophagus. This baby made a rapid recovery within a month with posture after feedings, and radiological reexamination at five months showed the œsophagus and cardia to be normal both anatomically and physiologically.

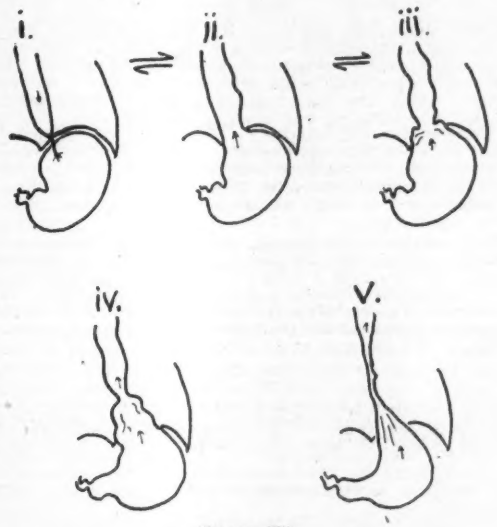

FIGURE III.

(i) Normal; (ii) simple cardio-œsophageal relaxation; (iii) minor intrathoracic stomach; (iv) intrathoracic stomach with short œsophagus and short stricture; (v) similar to type iv with a long narrow stenosis.

Case II.

W. first presented at the age of five months with symptoms of gastro-œsophagitis, similar to those described in Case I, which had been present since birth. Radiologically an irregularly widened œsophagus which filled readily by constant reflux was seen—the appearance of simple cardio-œsophageal relaxation (Figure V). Endoscopy revealed that the lower half of the œsophageal passage was lined with reddened and rugose mucosa which was interpreted as a short œsophagus and intrathoracic stomach. His vomiting decreased with medical supervision, but fourteen months later he had recurrence of vomiting of coffee-grounds material. A second X-ray examination gave the appearance of a threatening stricture, and widening of the lower end was now non-suggestive of intrathoracic stomach (see Figure VI). Endoscopy was repeated a week later under general anæsthesia and no stricture was present—the œsophagus was wider than usual with a completely lax hiatus, and on this occasion the mucosa appeared smooth and shining as far as the diaphragm. The child's clinical condition gradually improved, and at two years of age the radiological findings were still abnormal with reflux still present, though diminished—there was no stricture, but ballooning of the lower end of the œsophagus (or stomach) was present. The child has been quite well since, and was last heard of by letter at the age of six years, having moved to another State.

Case III.

B. in 1942 was first examined at the age of eight months with symptoms of gastro-œsophagitis similar to those in the previous cases. Radiologically reflux was seen with expansion above the diaphragm (see Figure VIII), while endoscopically the mucosa was seen to change to congested rugose mucosa in the lower half, as in Case II, and a diagnosis of congenital short œsophagus with an intra-

thoracic stomach was made. As the patient continued to vomit and lost weight during his two months' stay in hospital, his mother took him home against medical advice and nursed him herself. After the age of three years he ceased to vomit, and when reviewed at fourteen years of age he was still free of all symptoms, while X-ray examination revealed a normal œsophagus with no reflux or herniation.

Case IV.

R. was first examined at thirteen months of age with a clinical story similar to those of the preceding cases, but with milder symptoms. Fluoroscopy showed free reflux with a mobile cardia which could be observed to slip easily above and below the diaphragm at the first examination (Figures IX and X). At five and a half years of age he was very well, attending school, a very active child with a good healthy schoolboy appetite.

Case V.

E. was nine weeks old when she presented with a history of vomiting with blood streaking of the vomitus since birth. X-ray examination revealed constant reflux with a short stricture (Figure XI), while endoscopy showed a stricture, through which the œsophagoscope was not passed, and mucosal ulceration at one edge of the sphincter. At five months she was still vomiting a good deal, though gaining weight well. X-ray examination at this time still showed very free reflux, but a good calibre at the site of the former stricture and some widening distally above the diaphragm. On endoscopy a stricture was still said to be present (Figure XII).

When eighteen months old, the child was taking a full solid diet and sharing the meals of the family as they were served. At two and a half years she was a really lovely child, beautifully developed and free of symptoms. Her mother was a particularly intelligent and well-balanced person who managed the child with patience and attention to posturing and running about after meals.

Case VI.

M. at five months had gastro-œsophagitis, and the X-ray films showed a short œsophagus, intrathoracic stomach and stenosis (Figure XIII). On œsophagoscopy a stricture was seen which could not be passed. After treatment in hospital for two months the child improved clinically and there was some increase in the calibre of the stenosis (Figure XIII, right side).

The child's condition continued to improve slowly and she had trebled her birth weight at eleven months. Another episode of vomiting with blood staining of the vomitus caused the parents to seek surgical aid, and surgical repair of the hernia was carried out. Her subsequent progress was satisfactory, though the patient is not entirely free of vomiting episodes.

She represents the borderline type of case in which the decision between medical and surgical measures is difficult, and further experience of conservative treatment is necessary to establish a firmer base-line of comparison. In post-operative X-ray films of this child her stomach was seen to be well below the diaphragm with a narrowed hiatal canal in normal position. A small amount of reflux was persistently present after operation, but during the following twelve months this reflux increased considerably. This is not surprising if the diaphragmatic pinchcock plays a secondary role in the normal prevention of reflux. Any damage to the intrinsic mucosal mechanism would not be directly affected by diaphragmatic repair, and one can only speculate on the effects of mobilizing the œsophagus and freeing it of adhesions with possible interference with the vegetative nerve supply. In her post-operative course this child showed similar features to some of those conservatively treated—for example, Case II, in which free reflux persisted after the subsidence of œsophagitis and yet was associated with satisfactory clinical progress.

Further interest is attached to this patient in that she was examined for the same symptoms when only eight weeks old. No reflux or any convincing hernia was demonstrated, but when filled by barium the lower fourth of the œsophagus appeared irregular and a little widened, as in Figure XIV. Three months later an undoubted hernia, with free reflux, was present. One explanation given is that the condition was one of congenital short œsophagus with intrathoracic stomach, but as no reflux was present the latter could not be properly distended for radiological demonstration.

There may be an alternative explanation that the intrathoracic stomach was not seen at the first examination because it was not then present. The baby had marked symptoms of gastrœsophagitis, and the irregularity observed may have been due to inflammatory mucosal swelling which caused initial spasm of the cardia with subsequent reflux by involving the mucosal valve or the *muscularis mucosæ* which motivates the valve. Persistent inflammation and reflux could result in secondary shortening of the œsophagus and hiatus hernia.

Case VII.

J. was a girl of six years with symptoms of vomiting and hæmatemesis recurring periodically since birth, but during the last three years showing increasing pallor, dysphagia and failure to gain weight.

The first examination revealed a long narrow stricture, constant in several films of which two are shown in Figure XIV AA. After ten weeks' treatment with ulcer diet, sedation and posturing, she gained weight and managed a full ward diet without any dilatation being necessary. X-ray examination then showed considerable improvement in the lumen of the stricture (Figure XIV BB). Œsophagoscopy had revealed intense reflux œsophagitis, and the œsophagoscope was able to pass down the narrowed segment which was therefore not fibrosed.

The child was then taken home, but as she was one of a large family in a remote country area it was difficult to ensure continuity of good medical supervision, and she quickly relapsed with severe anæmia and malaise. After readmission to hospital she failed to respond adequately to medical treatment which was prolonged for six months in a convalescent home. Surgical treatment was therefore advised, and reduction of the hernia with vagal section and hiatal repair were carried out.

Her clinical progress after operation was excellent, with good steady gain in weight and no further bleeding or anæmia during the ensuing eighteen months, although her mother stated that she was still vomiting as before. Radiologically she still had very free reflux, but the œsophageal lumen was much wider, though irregular and atonic, while the stomach was well below the diaphragm.

There is no doubt that improvement was maintained for longer after surgical repair than with medical treatment in this case. The repaired hiatus has not stopped reflux. The questions are whether vagotomy has any effect on the bleeding mucosa or whether mobilization of the œsophagus and freeing of the periœsophageal adhesions have had any beneficial effect.

Case VIII.

R. was first examined nine years ago at the age of three weeks with projectile vomiting. Films showed a large intrathoracic stomach with short œsophagus (Figure XVI). She was regarded at the time as having a congenitally short œsophagus. At five months she was again examined by X rays. She had thriven well and the œsophagus was now seen to be normal in length and the stomach could be seen slipping above and below the diaphragm. No reflux was present. When two years old the child was free of all symptoms and was developing normally, and on repetition of the X-ray examination no herniation or reflux was demonstrable.

This was a case of spontaneous reduction which was still maintained at six and a half years of age, when the patient was last examined.

This case was included to illustrate the fact that a fairly large hiatal deficiency may be present in infancy without necessarily causing reflux, and the spontaneous anatomical restoration of the hiatal region is of interest.

Discussion.

Two and a half years ago 35 patients suffering from cardio-œsophageal relaxation or small hiatus hernia had been examined at the Royal Children's Hospital, presenting with symptoms during their first year of life. They had been followed for varying periods of one to five years, and all but one had run a benign clinical course. This one child had persistent symptoms and developed a large chronic peptic ulcer in the gastric hernia which was

recently excised at the age of six and a half years. This series agrees closely with the experience of Carré, Astley and Smellie.

Our experience of the clinical stages preceding fibrous stricture formation is small, for most of the patients treated at the Royal Children's Hospital for strictures complicating hiatal herniæ first present themselves in the older age groups. Despite the frequent dating of symptoms from early infancy, close investigation and management during the important first months or year or two of life have been limited. It is therefore difficult to determine which factors are responsible for the occasional case deviating from the usual benign course and progressing to the unpleasant complications of fibrous stricture or chronic ulcer formation.

The selection of cases discussed in this paper was made primarily to demonstrate some aspects of the clinical course of these conditions in childhood. Several conclusions may be drawn from a study of these cases.

1. A hiatal defect may be present early in life without necessarily causing reflux, as in Case VIII.

2. A condition of simple cardio-œsophageal relaxation or of minor intrathoracic stomach may return to normal after the symptoms of reflux and gastroœsophagitis have subsided if control is started early enough — for example, Cases I and III. Hiatal deficiency in the absence of pathological change in the mucosa does not appear to be the determining factor in causing reflux.

3. Reflux may persist long after the symptoms have subsided under medical control, and also after surgical treatment in which adequate hiatal repair has been carried out. This reflux may yet be compatible with satisfactory clinical improvement and no œsophagitis.

4. The diagnosis of actual or impending fibrous stricture and its differentiation from narrowing of the œsophagus due to spasm or œdema are difficult in a young child. Radiological examination may be misleading, for narrowing due to muscle spasm or œdematous infiltration of the submucosal tissues may persist with an unchanged picture for several weeks. In Case VII ten weeks elapsed before demonstrable improvement in the lumen was shown radiologically. Œsophagoscopy under anæsthesia helped in this case to show that the apparently narrow stricture would allow the passage of the œsophagoscope. In Case II also the appearance of a threatening stricture on X-ray examination was shown to be abolished on passage of the œsophagoscope. On the other hand, in Case V the second endoscopic examination suggested the persistence of a stricture, though radiologically a reasonable lumen could be demonstrated, and the child's subsequent good progress left no doubt that the narrowing, whatever its cause may have been, had cleared. Clinical study shows no direct parallel between the degree of dysphagia and severity of a stricture, except in advanced cases, for dysphagia may occur with œsophagitis and a wide atonic œsophagus in the absence of any stricture, and alternatively dysphagia may be masked in the case of a mild stricture by thorough mastication and slow eating habits. Careful correlation between clinical, radiological and endoscopic findings must be combined with a reasonable period of close clinical observation in order to make an accurate diagnosis.

The pathological sequence in infancy is unknown. It was assumed that congenital shortening of the œsophagus caused reflux and secondary mucosal changes resulting in bleeding and vomiting. Others contended that hiatal deficiency was the primary defect and that the mechanical effect of mobility caused congestion and bleeding from the mucosa, which was later explained by reflux œsophagitis.

The dating of symptoms of vomiting and bleeding from birth supported these hypotheses, but two other facts are not so easily explained: first, the rarity of short œsophagus uncomplicated by periœsophagitis in neonatal post-mortem material, of which larger series are now being more closely studied than previously; and secondly, the observation that radiological examination of vomiting infants sometimes gives negative results in the very young subject, yet may be followed by demonstration of a small gastric hernia and reflux at a later examination.

In 1950 Gruenwald published the results of 310 consecutive neonatal post-mortem examinations, in which sections were made of the œsophago-gastric region in all cases. Of this number, 52 showed ulceration or mucosal changes which he described as acute œsophagitis, and this, he suggested, should be considered as a cause of vomiting and hæmatemesis in the newly born, after the exclusion of bleeding diseases. Several factors, such as birth trauma, neonatal asphyxia and tube feeding, were considered in the ætiology of this condition, but one interesting fact emerged from the study, that no instance of œsophageal shortening or hiatal deficiency was present in this series. It would seem, therefore, that the incidence of non-specific œsophagitis (this term being used to distinguish it from reflux œsophagitis) is much commoner than any congenital abnormality of this region. Pathological studies in larger series of adults by K. V. Lodge and P. M. Peters also show a wide incidence of œsophagitis beyond those associated with hiatus hernia.

Gruenwald's studies suggest, therefore, that vomiting with hæmatemesis in the neonatal period, after exclusion of hæmorrhagic disease, is more likely to be associated with œsophagitis than with an established anatomical abnormality. It is conceivable that if vomiting and œsophagitis do not subside, cardiac incompetence could develop with subsequent reflux œsophagitis and herniation. The findings in Case VI were given as a possible instance of this sequence.

While it is not suggested that endoscopy is warranted as a routine for investigation of these young vomiting babies, a planned study of a small number of cases if controlled with biopsy could yield further data of value. Until the pathological basis of the mucosal changes of the gastro-œsophageal region is clarified, both endoscopic and radiological interpretation in the early stages of these clinical conditions must remain limited in their scope.

Acknowledgements.

Acknowledgement is made to members of the senior medical staff and to the surgical director of the Royal Children's Hospital, Mr. Russell Howard, for the opportunity of radiological study of the cases discussed.

References.

ALLISON, P. R (1951), "Reflux Esophagitis, Sliding Hiatal Hernia, and the Anatomy of Repair", *Surg., Gynec. & Obst.*, 92: 419.

ASTLEY, R., and CARRÉ, I. J. (1954), "Gastro-Œsophageal Incompetence in Children, with Special Reference to Minor Degrees of Partial Thoracic Stomach", *Radiology*, 62: 351.

CARRÉ, I. J., ASTLEY, R., and SMELLIE, J. M. (1952), "Minor Degrees of Partial Thoracic Stomach in Childhood. Review of 112 Cases", *Lancet*, 2: 1150.

CREAMER, B. (1955), "Œsophageal Reflux", *Lancet*, 1: 279.

DORNHORST, A. C., HARRISON, K., and PIERCE, J. W. (1954), "Observations on the Normal Œsophagus and Cardia", *Lancet*, 1: 695.

DUHAMEL, B., and MASSE, N. P. (1953), "*Les anomalies de fonction et de position du cardia chez le nouveau-né*", *Et. néonatal.*, 2: 163.

FINDLAY, L., and KELLY, A. B. (1931), "Congenital Shortening of the Œsophagus and the Thoracic Stomach Resulting Therefrom", *J. Laryng. & Otol.*, 46: 797.

GRUENWALD, P., and MARSH, M. R. (1950), "Acute Esophagitis in Infants", *Arch. Path.*, 49: 1.

JOHNSTONE, A. S. (1955), "Œsophagitis and Peptic Ulcer of the Œsophagus. The Mackenzie Davidson Memorial Lecture (November 25, 1954)", *Brit. J. Radiol.*, 28: 229.

LODGE, K. V. (1955), "The Pathology of Non-Specific Œsophagitis", *J. Path. & Bact.*, 69: 17.

NEUHAUSER, E. B. D., and BERENBERG, W. (1947), "Cardio-Esophageal Relaxation as a Cause of Vomiting in Infants", *Radiology*, 48: 480.

PETERS, P. M. (1955), "The Pathology of Severe Digestion Œsophagitis", *Thorax*, 10: 269.

PLARRE, F. (1953), "The Syndrome of Cardio-Œsophageal Relaxation. Radiological Features" (Melbourne Pædiatric Society Meeting, March 11, 1953), M. J. AUSTRALIA, 2: 115.

WYLLIE, W. G., and FIELD, C. E. (1946), "The Etiology of Intermittent Œsophageal Regurgitation and Hæmatemesis in Infants", *Arch. Dis. Childhood*, 21: 218.

Legends to Illustrations.

FIGURE IV.—Case I. Four serial films showing constant reflux.

FIGURE V.—Case II at five months. Filled by reflux.

FIGURE VI.—Case II; the patient's age is nineteen months.

FIGURE VII.—Case II; the patient's age is two and a half years.

FIGURE VIII.—Case III; the patient's age is eight months.

FIGURE IX.—Case IV; the patient's age is eleven months.

FIGURE X.—Case V; the patient's age is nine weeks. Serial films filled by reflux show constant stricture.

FIGURE XI.—Case V; the patient's age is five months.

FIGURE XII.—Case VI: AA when the patient was aged five months; BB when the patient was aged eight months.

FIGURE XIII.—Case VI; the patient was aged eight weeks. Film on right filled by "swallow".

FIGURE XIV.—Case VII; the patient was aged six years. AA = first examination. BB = ten weeks later.

FIGURE XV.—Case VIII; the patient was aged three weeks.

FIGURE XVI.—Case VIII.

USE OF RHESUS-POSITIVE BLOOD IN EXCHANGE TRANSFUSION FOR HÆMOLYTIC DISEASE OF THE NEWBORN.[1]

By S. E. L. Stening,
Sydney.

The treatment of hæmolytic disease of the newborn has been fraught with disappointments for many of us—not only for pædiatricians, but for the obstetrician, who has the mortification of losing infants in the neonatal period and also from stillbirth.

It is conceivable that in the near future deaths from stillbirth and *hydrops fœtalis* will be much reduced in frequency or prevented altogether. But at present it is the problem of salvaging all live-born babies suffering from hæmolytic disease which is most pressing and immediate. May I add that "salvage" means recovery without sequelæ.

In live-born infants suffering from hæmolytic disease there are several main manifestations, upon which the decision to commence early and adequate therapy depends. Early and adequate therapy means early and adequate exchange transfusion. These manifestations are:

1. Anæmia. Unless the infant is markedly anæmic at birth, for instance a cord hæmoglobin value of eight grammes *per centum* or less, anæmia is not a serious difficulty. Consideration of accompanying signs must take precedence; these are jaundice, toxic signs and maturity.

2. Toxic signs. Puffiness or frank œdema, purpura or other evidence of hæmorrhage, and abdominal distension with or without gross enlargement of the liver and spleen are often present together and betoken a severe affection.

3. Maturity. There is no doubt that the risk of death and complications is higher in the smaller infants. This sign alone may sometimes be an indication for prompt therapy.

4. Jaundice. Jaundice may not be present in the mildest cases at any stage or in the severest—those hydropic infants who die before jaundice has time to appear. In all other sufferers the appearance of jaundice must be anticipated, watched for and studied as it develops. This is because jaundice appears to be the most difficult manifestation to control and its complications are so distressing. Affected infants, whether treated or untreated, who develop severe grades of jaundice are exposed to the hazard of kernicterus. The appearance of undoubted signs of kernicterus means that the infant may die within a few hours or, if the infant recovers, there may be a later development of severe neurological signs, which are a permanent and severe handicap.

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 13 to 16, 1956.

The unfortunate sufferer is a burden to his family and a pitiful object to those around him, no matter what his intelligence may be.

Exchange transfusion and repeated exchange transfusions have significantly reduced the incidence of kernicterus in several reported series. However, even after exchange transfusion kernicterus has developed. Allen *et alii* (1950) state:

> The liberal use of exchange transfusion has apparently been additionally responsible in part for the nearly complete disappearance of Kernicterus as a complication . . .

And in a footnote in the same paper they add:

> The baby . . . 30 weeks gestation. . . . In spite of two exchange transfusions within the first 24 hours of life, jaundice became severe and definite clinical evidence of Kernicterus developed.

These quotations indicate that an occasional infant may suffer kernicterus as the result of hæmolytic disease of the newborn, especially if premature, in spite of adequate treatment by exchange transfusion.

My experience of exchange transfusion began in 1948. Since then all types of hæmolytic disease of the newborn have been encountered, from the severest to the mildest, in large babies and in tiny ones. When exchange or simple transfusion was employed rhesus-negative blood was used exclusively until, in 1954, a mother who had previously borne an affected infant, which survived but suffered kernicterus, was delivered of another infant. This infant was treated by exchange transfusion, apparently adequate, but within forty-eight hours this infant was also in the throes of kernicterus. He too survived, leaving that mother with two severely impaired and spastic infants to look after. I was greatly distressed at this failure.

It appeared necessary, then, to search for alternative or modified methods of treatment in an effort to avoid repetition of such a tragedy.

Ætiology.

Gerrard (1952) has stated the six main hypotheses in the ætiology of kernicterus:

> (i) Agglutination thrombi block terminal capillaries.
>
> (ii) Result of antigen-antibody reaction between Rh antibody and Rh positive nerve cells.
>
> (iii) An anaphylactic reaction which only occurs in the sensitized subject.
>
> (iv) An hepatic encephalopathy.
>
> (v) After reviewing the above, Claireaux (1950) concluded that the only adequate cause for cerebral damage is the associated anæmia and anoxia.
>
> (vi) Bilirubin, itself, in excess. Produced experimentally in the experimental animal by intravenous injection of bilirubin to the level of 100 to 150 milligrammes per 100 millilitres.

Gerrard concluded by stating:

> The general concensus of opinion, both before the discovery of the Rh factor, and since, has agreed with Bencke (1907) that pigmentation of the brain is secondary and that the nerve cells are first damaged by a factor or factors unknown.

As far as is known to me, there have been no further significant thoughts on the ætiology of kernicterus since then, except for the implication of the indirect type or fraction of the serum bilirubin as the causative factor.

If one examines the hypotheses enumerated above, certain possible causative factors come to mind.

(i) Agglutination thrombi. This suggestion has been withdrawn by its proposers in the absence of histological confirmation.

(ii) Antigen-antibody reaction in nerve cells. The idea that this is operative has never been completely refuted in the hæmolytic disease of the newborn, but it is difficult to accommodate this hypothesis to those cases of kernicterus which occur without any evidence of sensitization or blood incompatibility. It is still possible, however, that some so far undiscovered factor akin to the Rh factor may be present in these cases.

(iii) An anaphylactic reaction which occurs only in the sensitized subject. This hypothesis was put forward in an endeavour to explain the relative infrequency of kernicterus. It is related to (ii) above and is subject to the same criticism *plus* the fact that local (neuronal) anaphylaxis is less likely than a generalized reaction. But if local anaphylactic reactions do occur, then one would expect these reactions to be even rarer than they are.

(iv) Hepatic encephalopathy. Liver damage undoubtedly occurs in severely jaundiced infants and is manifested by inefficient excretion of bilirubin. It is not easy for me to envisage a toxin, produced in the damaged liver, which could cause damage in such a selective area.

(v) Cerebral damage due to associated anæmia and anoxia. The idea that this is operative can be criticized in that anoxic damage would be general and the symptoms similar to those observed in non-kernicteric infants, who might be similarly exposed. Secondly, and more important, infants develop kernicterus in the absence of anæmia, and, as far as can be assessed, in the absence of intra-uterine, intra-partum or post-partum anoxia.

(vi) Bilirubin, whether total or only indirect type of bilirubin as the cause. Undoubtedly bilirubin is essential to the appearance of kernicterus. There is also no doubt that the percentage of affected infants will rise with increases in the intensity of jaundice. But this hypothesis fails to explain the development of kernicterus at a level of nine milligrammes *per centum*. This occurrence has been personally observed in a premature infant and confirmed by post-mortem examination. It also fails to explain why kernicterus did not develop at a level of 38 milligrammes *per centum* in Case 29 of the present series.

My observations lead me to believe that there are other factors involved in the pathogenesis of kernicterus, apart from any of the hypotheses mentioned so far. One of these may be a genetic factor, since one has knowledge of several families in which two or more infants suffered or died from kernicterus. Likewise one has knowledge of families in which there has been a decided tendency to hydrops, and others still in which there has been a long succession of mildly affected infants.

In hæmolytic disease of the newborn, if we allow for exposure to anoxic factors and even for varying grades of maturity and weight, there does seem to be an increased susceptibility in some infants.

Hsia *et alii* (1952) have produced evidence to show the increasing incidence of kernicterus as the serum bilirubin increases. This finding is not disputed. Here are their figures:

Serum Bilirubin Level.	*Incidence of Kernicterus.*
0- 5 milligrammes per 100 millilitres	0
6-15 milligrammes per 100 millilitres	3%
16-30 milligrammes per 100 millilitres	18%
Over 30 milligrammes per 100 millilitres	50%

It has still to be explained why so many infants whose serum bilirubin content exceeded 16 milligrammes *per centum* failed to develop kernicterus, and particularly why only 50% of infants whose serum bilirubin content exceeded 30 milligrammes *per centum* developed the condition.

What protected the unaffected 50%?

It seems that there is an unknown susceptibility or an unknown protective factor, which makes some infants more liable and some more resistant to kernicterus. Boorman and Dodd (1943) have demonstrated that tissue cells contain Rh antigens. This has been confirmed by Brading and Walsh (1954), who stated that the lesions in the brain and liver were due "to the injurious effect of the union of antibody and antigen on the tissue cells of the organ and not on the red cells . . . . This elution (of antibody by exchange transfusion) is not complete because infants dying after replacement transfusion have still had antibody adherent to tissue cells. The question must therefore be raised as to whether a more active elution of tissue antibody would not be achieved *in vivo* if Rh-positive blood were transfused."

Exchange Transfusion.

Since I had no way of knowing which infants, at birth or soon after, affected by hæmolytic disease were going to be more resistant or more susceptible to the development of kernicterus, it was decided to investigate the possibility of preventing kernicterus by using rhesus-positive blood in exchange transfusion for hæmolytic disease of the newborn.

Herewith are the results of a year's exclusive use of Rh-positive blood for exchange transfusion in hæmolytic disease. These results may be directly contrasted with parallel figures from the preceding year, July 1, 1953, to June 30, 1954.

TABLE I.

Group.	Year Ending June 30, 1954.[1]	Year Ending June 30, 1955.[2]
Rh-negative mothers without agglutinins	667	657
Rh-negative mothers with agglutinins	71	71
Affected babies (Coombs-positive)	54	61
Unaffected babies (Coombs-negative)	17	10
Babies:		
Exchange transfusion only	19 } 32	20 } 38
Exchange transfusion *plus* ordinary	13 }	18 }
Ordinary transfusions only	10	3
Coombs-positive. No transfusion	12	20
Deaths after exchange transfusion	5 } 6	2 } 4
Deaths before exchange transfusion	1 }	2 }
Kernicterus	2	1
Multiple exchange transfusion	1	11

[1] In this year Rh-negative blood was used exclusively.
[2] In this year Rh-positive blood was used exclusively.

In the test year July 1, 1954, to June 30, 1955, a total of 71 mothers were admitted to the hospital who were found to be Rh-negative and who had agglutinins in their blood. Of these 71 mothers, no less than 10 had infants whose blood failed to react to the Coombs test and were unaffected. Of the remaining 61, 38 had exchange transfusion with rhesus-positive blood. Of these, two died. One of these was an hydropic infant, who succumbed soon after the transfusion had begun at thirty minutes of age. The other, whose history will be appended, died at fifty-three hours during its second exchange transfusion.

Three infants had simple transfusions only; of these, none died. Eighteen infants were so mildly affected that no transfusion was given; there were no deaths. There were two infants who died without transfusion. One suffered from massive hydrops and lived only about twenty minutes, and the other, a tiny premature infant of one pound thirteen ounces, who was thought to be too frail for treatment, died at twenty-five hours of age.

The one case of kernicterus occurred in the infant that died during its second exchange transfusion. Kernicterus was not suspected during life and, since the infant had other lesions, was probably not the sole cause of death.

It is noteworthy that 11 infants received multiple exchange transfusions (see Table II). Quite a large proportion of babies transfused with rhesus-positive blood

TABLE II.

Type of Transfusion.	Numbers.
1 exchange transfusion	15
1 exchange transfusion *plus* 1 simple transfusion	7 } 27
1 exchange transfusion *plus* 2 simple transfusions	5
2 exchange transfusions	5
2 exchange transfusions *plus* 1 simple transfusion	4 } 9 } 38
3 exchange transfusions	0
3 exchange transfusions *plus* 1 simple transfusion	0 } 2
3 exchange transfusions *plus* 2 simple transfusions	2

became severely jaundiced, so jaundiced that one had to give them the benefit of further exchange transfusion. In spite of this high degree of jaundice only the infant described above had kernicterus.

Several infants were noted to have neurological signs during the first five days of life. These signs were irritability, lethargy and some arm movement. These infants were those of Cases 23, 29, 33, 8, 9, 35, 32, 22, 14. At a follow-up all these babies except numbers 14 and 8 were actually seen. All were well and their development was assessed as normal. There were no signs suggestive of previous kernicterus. In Case 8 the baby gave a negative result to the Coombs test; he did not receive a transfusion and his serum bilirubin content rose to 22 milligrammes *per centum*. Follow-up was not done in this case.

The follow-up was carried out in February, 1956, which allowed a minimum period of eight months to elapse between treatment and the follow-up. Most of the infants were seen on this follow-up day, when independent opinions on their physical state were available. The condition of those who did not report on that day was assessed from the parents' replies to a *questionnaire*.

Table III is given to illustrate the numbers of affected infants over the last twelve years, the increase in the numbers of exchange transfusions, and the apparent increase in the numbers of stillbirths in latter years, in spite of induction of labour in many severe cases.

Table III.

Year.	Total Affected Hæmolytic Disease of Newborn.	Exchange Transfusion.	Simple Transfusion Only.	Stillbirth.	Died.
July 1, 1943, to June 30, 1944	8	0	5	?	1
July 1, 1944, to June 30, 1945	15	0	12	?	2
July 1, 1945, to June 30, 1946	8	0	6	?	2
July 1, 1946, to June 30, 1947	33	0	17	?	12
July 1, 1947, to June 30, 1948	26	6	13	4	6
July 1, 1948, to June 30, 1949	27	8	20	9	7
July 1, 1949, to June 30, 1950	24	13	8	7	2
July 1, 1950, to June 30, 1951	48	16	20	6	7
July 1, 1951, to June 30, 1952	63	25	30	4	14
July 1, 1952, to June 30, 1953	60	21	20	6	10
July 1, 1953, to June 30, 1954	54	32	10	8	6
July 1, 1954, to June 30, 1955	61	38	3	10	4

Conclusions.

While it is realized that the number of treated infants is too small to be of great significance, it does appear from the results and from comparison with previous years that the use of rhesus-positive blood is not harmful.

Secondly, the use of rhesus-positive blood in exchange transfusion for hæmolytic disease of the newborn does not increase the liability to kernicterus, especially when repeated exchanges are made.

Thirdly, supplementary exchange transfusion will be required more often when this type of blood is used, rendering the method less suitable for premature infants and those who are ill because of some other complication of birth.

Fourthly, a serum bilirubin level of 38 milligrammes *per centum* produced by this type of blood is not necessarily productive of kernicterus.

Fifthly, more experience is required, covering large numbers of affected infants, more particularly the severely affected.

Finally, efforts will have to be made to salvage those infants who are stillborn or who are born severely affected and die within an hour of birth, usually during the exchange transfusion.

Acknowledgements.

I wish to acknowledge the cooperation extended by all members of the obstetric staff of the Women's Hospital, Crown Street, Sydney, for allowing me to carry out this investigation on their patients. I also wish to acknowledge the helpful criticism and advice of Dr. M. Moyes, pathologist to the hospital, and to thank those members of the resident staff who actually performed all the transfusions and who so loyally helped.

Finally, I wish to acknowledge the gentle push by Dr. R. J. Walsh, of the Red Cross Blood Transfusion Service, Sydney, which sent me on with this investigation when I was wavering.

References.

Allen, F. H., Diamond, L. K., and Vaughan, V. L. (1950), "Erythroblastosis Fetalis; Prevention of Kernicterus", *Am. J. Dis. Child.*, 80: 779.

Boorman, K. E., and Dodd, B. E. (1943), "Group-Specific Substances, A, B, M, N and Rh; Their Occurrence in Tissues and Body Fluids", *J. Path. & Bact.*, 55: 329.

Brading, I., and Walsh, R. J. (1954), "The Role of Tissue Antigens in Hæmolytic Disease of the Newborn", *Australian J. Exper. Biol. & M. Sc.*, 32: 213.

Gerrard, J. (1952), "Kernicterus", *Brain*, 75: 526.

Hsia, D. Y-Y., Allen, F. H., junior, Gellis, S. S., and Diamond, L. K. (1952), "Erythroblastosis Fetalis. VIII: Studies on Serum Bilirubin in Relation to Kernicterus", *New England J. Med.*, 247: 668.

Appendix I.

History of Case 41.

The mother's obstetric history is as follows. She had had seven normal pregnancies resulting in eight normal and unaffected infants. She had had two premature stillbirths. This pregnancy, her first in this country, was complicated by hypertension in the mother and the presence of anti-Rh agglutinins to the titre of one in 64 in albumin. The infant was delivered by Cæsarean section at thirty-seven weeks' gestation. At birth the infant was only moderately pale and there was no clinical jaundice. The cord bilirubin content was 3·1 milligrammes *per centum*, and the capillary hæmoglobin 18·2 grammes *per centum*. There were seven late normoblasts per 100 white cells. The liver was palpable two fingers' breadth below the costal margin, and the spleen could just be felt. There were no petechiæ. The abdomen was described as full. This infant was regarded as being mildly to moderately affected, but since the cord bilirubin content exceeded 3·0 milligrammes *per centum* and the weight was only four and three-quarter pounds, exchange transfusion with rhesus-positive blood was carried out at two hours of age. Seven hundred and fifty millilitres were removed and 720 millilitres were given over a period of ninety-five minutes. The infant's condition throughout was good.

Jaundice was first noted at twenty hours of age, and this jaundice increased in severity. After exchange transfusion, the bilirubin content was 2·1 milligrammes *per centum*. At twenty-four hours it was 16·8 milligrammes *per centum*. There was some suggestion of neck stiffness and increased tone in the legs at twenty-four hours of age. Wavering movements of the arms were reported at twenty-six hours of age. Owing to misunderstanding, no further bilirubin estimations were made until forty-eight hours of age, when a figure of 36·8 milligrammes *per centum* was obtained. The second belated exchange transfusion was then begun, but after only eighteen minutes of the procedure, the infant's respirations suddenly became slow and weak. The transfusion was stopped, but the infant failed to rally and died thirty minutes later.

Autopsy in this infant revealed "slight and sometimes moderate chromatolysis of moderately numerous neurons in some nuclei of the brain, with normal neurons in many other cerebral nuclei".

The pathologist's summing up was as follows:

> The cause of death in this infant was not revealed at autopsy. The positive findings, viz: moderate congestion of the pulmonary vessels, patchy slight pulmonary œdema, slight pulmonary emphysema and kernicterus, probably all contributed to the child's death, but neither alone nor in combination were these signs sufficient to account for death, particularly the mode of death indicated in the clinical history. A possible cause of death, . . . is coronary embolus via the patent *foramen ovale*.

Appendix II.

Case Summaries and Follow-Up.

Case Number.	Birth Weight. (Pounds and Ounces.)	Coombs Test Result.	First Hæmoglobin. (Grammes *per Centum.*)	Cord Bilirubin. (Milligrammes *per Centum.*)	Highest Bilirubin Content.	Assessment.	Type of Transfusion.	Result.	Follow-Up.
1	6 11½	+	22·9	1·4	?	Mild.	0	Well.	Very well.
2	5 6½	+	20·4	0·3	5·8	Mild.	0	Well.	Well, but eczema, allergic to orange.
3	6 8½	−	21·0	—	—	Unaffected.	0	Well.	Nil.
4	7 14½	−	23·4	—	—	Unaffected.	0	Well.	Nil.
5	5 14½	+	19·0	1·6	10·8	Mild.	0	Well.	Normal.
6	7 3	−	20·7	—	—	Unaffected.	0	Well.	Nil.
7	5 0½	+	20·3	2·0	17·7	Moderate.	0	Well.	Did not report.
8	5 1½	−	17·6	—	22·0	Unaffected.	0	Well.	Nil.
9	5 0½	+	17·9	1·8	15·3	Moderate.	1 exchange, 2 simple.	Well.	Normal.
10	5 8½	−	19·1	—	—	Unaffected.	0	Well.	Nil.
11	6 8½	−	21·2	—	—	Unaffected.	0	Well.	Nil.
12	7 5½	+	21·0	2·5	—	Mild.	0	Well.	Normal.
13	5 15	+	18·8	5·6	26·2	Severe.	2 exchange, 1 simple.	Well.	Normal.
14	7 2½	+	13·6	4·7	5·1+	Moderate.	1 exchange, 1 simple.	Well.	Normal.
15	7 7½	+	14·4	5·2	6·8+	Moderate.	1 exchange.	Well.	Did not report.
16	6 1	+	21·9	4·1	24·1	Severe.	1 exchange, 2 simple.	Well.	Normal.
17	9 0	+	14·4	3·0	8·5	Severe.	2 exchange.	Well.	Normal.
18	7 6½	+	6·7	2·8	4·8	Severe.	1 exchange, 2 simple.	Well.	Normal. Holds breath.
19	5 12½	+	9·7	5·4	9·0	Severe.	2 exchange, 1 simple.	Well.	Bronchitis, vomits milk.
20	4 14½	+	18·8	4·7	5·2+	Moderate.	1 exchange.	Well.	Did not report.
21	7 14½	+	17·6	3·3	6·3	Moderate.	1 exchange.	Well.	Normal.
22	4 14½	+	10·0	—	4·3	Moderate.	1 exchange, 2 simple.	Well.	Bronchitis, otherwise normal.
23	5 2½	+	21·3	2·8	8·0	Moderate.	1 exchange.	Well.	Normal, had pneumonia.
24	6 14½	+	13·5	3·9	9·0	Severe.	1 exchange.	Well.	Bronchitis, otherwise normal.
25	5 4½	+	—	—	—	Very severe.	Part exchange.	Died.	
26	7 14	+	16·4	3·5	9·4	Mild.	1 exchange.	Well.	Normal.
27	5 14½	+	10·7	3·3	4·9	Moderate.	2 exchange.	Well.	Normal, allergic to insect bites.
28	7 11½	+	16·2	3·1	5·3	Mild.	1 exchange.	Well.	Normal.
29	5 6½	+	10·7	8·0	38·0	Very severe.	3 exchange, 2 simple.	Well.	Normal.
30	6 11½	+	16·9	3·2	15·0	Severe.	1 exchange.	Well.	Normal.
31	7 1½	+	18·8	2·0	—	Mild.	0	Well.	Pale and weak. No nervous sign.
32	9 10	+	19·2	5·5	11·0	Severe.	2 exchange.	Well.	Normal. "Colds."
33	5 9½	+	14·4	4·6	13·0	Severe.	2 exchange, 1 simple.	Well.	Normal. Suspected pyloric. Allergic to penicillin.
34	6 1	+	17·6	4·6	—	Moderate.	1 exchange.	Well.	Normal.
35	5 10	+	13·2	6·2	9·0	Severe.	2 exchange.	Kernicterus suspected.	Normal.
36	7 11	+	17·2	3·6	—	Moderate.	1 exchange, 1 simple.	Well.	Did not report.
37	9 8	+	13·8	3·4	—	Moderate.	1 exchange.	Well.	Normal.
38	5 5½	+	23·2	2·3	12·4	Moderate.	1 exchange.	Well.	Normal.
39	8 9½	+	15·0	3·5	10·0	Moderate.	1 exchange, 1 simple.	Well.	Normal, but allergic to milk. Pneumonia.
40	6 5½	+	8·5 At 9 hours.	13·5	—	Severe.	1 exchange.	Well.	Bow legs only.
41	4 13½	+	18·2	3·1	36·8	Severe.	2 exchange.	Died.	Died during second exchange.
42	7 9	+	13·8	2·9	—	Moderate.	1 exchange, 1 simple.	Well.	Nervy. Hives.
43	6 5	+	15·2	2·3	8·1	Moderate.	1 exchange.	Well.	Did not report. Twin of Case 44, who did not report.
44	5 9	+	18·5	2·4	7·0	Moderate.	1 exchange.	Well.	
45	5 6	+	15·7	6·9	17·7	Severe.	2 exchange, 1 simple.	Well.	Normal.
46	6 12	+	16·6	6·6	—	Moderate.	1 exchange, 1 simple.	Well.	Did not report.
47	6 11	+	10·2	5·3	—	Severe.	1 exchange, 1 simple.	Well.	Normal. Eczema.
48	8 2½	+	16·7	3·7	12·6	Moderate.	1 exchange, 2 simple.	Well.	Normal. Eczema.
49	5 8½	+	14·4	4·8	18·0	Moderate.	1 exchange.	Well.	Normal, but "colds". Allergic to bites.
50	6 6	+	15·0	5·0	36·0	Very severe.	3 exchange, 2 simple.	Kernicterus suspected.	Normal.
51	6 5½	+	14·2	—	2·0	Mild.	1 simple.	Well.	Normal.
52	6 8	+	20·0	2·5	—	Mild.	0	Well.	Normal.
53	6 12½	+	18·0	3·6	15·0	Moderate.	0	Well.	Normal. "Colds."
54	6 5	+	18·2	1·3	3·0	Mild.	0	Well.	Pale.
55	6 8	−	22·0	—	—	Unaffected.	0	Well.	Not done.
56	5 8	+	24·1	—	—	Mild.	0	Well.	Did not report.
57	7 13	+	19·1	2·3	5·4	Mild.	0	Well.	Bow legs.
58	6 2	+	4·0	5·2	—	*Hydrops fœtalis.*	0	Died.	Died before transfusion.
59	7 2	+	24·0	3·2	9·5	Mild.	0	Well.	Did not report.
60	7 14	+	19·1	2·4	4·7	Mild.	0	Well.	Did not report.
61	6 9	−	21·3	—	—	Unaffected.	0	Well.	Not done.
62	7 8	+	19·3	4·6	6·5	Mild.	1 simple.	Well.	Anæmic.
63	7 1½	+	11·9	—	—	Mild.	1 simple.	Well.	Bronchitis. Eczema.
64	7 11	−	20·7	—	—	Unaffected.	0	Well.	Not done.
65	6 15	+	21·9	1·4	—	Mild.	0	Well.	Normal.
66	7 4	+	16·9	1·8	2·0	Mild.	0	Well.	Normal, but rashes and hives.
67	7 13½	+	19·7	—	—	Mild.	0	Well.	Hives.
68	7 10½	+	18·5	1·1	2·0	Mild.	0	Well.	Normal.
69	1 13	+	11·3	—	—	Moderate.	0	Died.	Untreated, very frail premature. No kernicterus.
70	6 8	+	17·4	1·3	—	Mild.	0	Well.	Normal.
71	5 8	−	21·0	1·0	—	Unaffected.	0	Well.	Not done.

A STUDY OF THE ANÆMIA FOLLOWING EXCHANGE TRANSFUSION IN HÆMOLYTIC DISEASE OF THE NEWBORN.[1]

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IT is well known that anæmia often occurs in the first months of life in infants who have had hæmolytic disease of the newborn. This anæmia may occur whether the infant has been treated with one or more exchange transfusions, whether it has had simple transfusions, or whether it has been untreated.

Since November, 1952, 54 infants have been treated by me with one or more exchange transfusions for hæmolytic disease of the newborn at Saint Margaret's Hospital for Women, Sydney. In 28 of these infants it has been possible to carry out serial hæmoglobin level estimations during the period of the anæmia. Physical and developmental progress has also been observed regularly in all and up to the age of twelve months or more in 20. Of the 28 infants, 22 showed a fall in hæmoglobin value which reached a minimum by the sixth week, the lowest levels encountered being six grammes *per centum*. The level then rose to what was considered to be a normal figure of 10 grammes *per centum* or more by the twentieth week at the latest and usually earlier. Two infants (Cases 2 and 11) early in the series were given one additional simple transfusion at the ages of two and four days, respectively, but the remainder received no treatment by means of simple transfusions, iron or other hæmatinics. The essential details of these infants are illustrated in the accompanying table (Table I). Figure I shows the typical change in hæmoglobin levels of eight patients.

During the period when anæmia was present, the infants were examined at weekly or fortnightly intervals. Pallor of the skin was noticeable, especially when the infant was asleep, but a pink colour appeared during crying. All infants sucked with vigour. In two cases breast feeding was not established, in one instance breast feeding was abandoned in the first month, in 12 cases it was abandoned between four and twelve weeks, in three between twelve and twenty weeks, and in 10 breast feeding was continued beyond this age and was then stopped by instruction. When breast feeding was abandoned earlier than twenty weeks, the reason was always failure of maternal supply and never anything to do with the infant.

When artificial milk feeding was introduced, the mixture was made from whole cow's milk, dried whole cow's milk or dried "humanized" cow's milk. The mixture was sufficiently strong to contain a proportion of cow's milk protein of at least 2%. Vitamin *C* was introduced when artificial mixtures were commenced or at the age of twelve weeks, whichever was the earlier. A water-soluble vitamin concentrate was given to supply vitamin *D* only when the artificial feed was made from whole cow's milk. Vegetable broth and cereal were introduced at the age of twelve weeks, egg at the age of sixteen weeks and all varieties of tinned proprietary strained foods at the age of twenty weeks. No iron in medicinal form was given to any infant. Weight gains were within normal limits and proportional to increases in length and head circumference. The weights at the ages of sixteen and fifty-two weeks are shown in the table.

During the period of the anæmia all infants appeared to be normally vigorous, crying in a normal fashion and sucking well. The usual motor advances in development appeared at the usual times. In Table I are shown the ages at which the head was held firmly erect, sitting was firm, and spontaneous pulling to the feet occurred, and when the infant could walk with one hand held.

There was no tendency to contract intercurrent illnesses. In Case 4 the child contracted the encephalitic form of acute poliomyelitis at the age of ten weeks from which she recovered, being left with a slight lower motor neuron weakness of one deltoid muscle. In Case 38 the infant was difficult to feed and was subject to frequent mild upper respiratory upsets. He has subsequently developed mild bronchial asthma.

No conclusions could be reached from this study as to why this anæmia develops. In the normal infant the hæmoglobin level falls at a diminishing rate, reaching its minimum between the ages of eight and twenty weeks, as shown in Figure II (Walsh *et alii*, 1953). During this period the bone marrow is inactive, the reticulocytes falling from a level of 2% to 3% of the red cells in the neonatal period, to a level of 0·1% to 0·2% by the eighth week and then rising to 0·5% to 2% in the twelfth week. In the patients in this series there was a rapid fall in the initial high percentage of reticulocytes; this was followed by a rise, which reached a maximum at the time when the hæmoglobin had fallen to its lowest level. As the hæmoglobin level rises again the percentage of reticulocytes again falls (Figure III). When the fall in hæmoglobin level is less marked, a reticulocytosis of such proportions does not occur (Figure IV). This reticulocyte response is much greater than that which occurs in the normal and indicates greater activity of the marrow in restoring the situation.

Another factor tending to cause a fall in hæmoglobin level in the normal and in the infants in this series is the increase in blood volume which necessarily accompanies increase in weight. Hyman and Sturgeon (1955) have shown that in the anæmia following hæmolytic disease of the newborn there is an increase in total hæmoglobin despite the fall in hæmoglobin levels.

It is believed that those of the infant's original sensitized red cells, which have not been replaced by exchange transfusion, will be hæmolysed during the four to eight weeks that maternal antibodies are present (Levine, Vogel and Rosenfield, 1953). The infant will then depend on red cells produced by its own bone marrow and the red cells introduced during exchange transfusion. The latter will be destroyed at such a rate that the hæmoglobin content will fall by 0·13 gramme *per centum* per day (Ashby, 1919). If the infant was not to produce its own red cells, the hæmoglobin level would fall from a post-exchange figure of 15 grammes *per centum* to 4·6 grammes *per centum* at the end of six weeks (Levine, Vogel and Rosenfield, 1953).

There should be some relationship between the severity of the anæmia following exchange transfusion and the severity of the original hæmolytic disease. If one accepts the level of hæmoglobin in the cord blood as the most accurate measure of severity (Mollison and Cutbush, 1951), one can compare the incidence and severity of the anæmia after exchange transfusion in those with a low cord hæmoglobin level with those with a comparatively high level. In Cases 28, 41, 52, 54 and 55 the cord hæmoglobin levels were 4·6, 7·2, 4·0, 7·2 and 4·5 grammes *per centum*. All these infants developed anæmia, the minimum level of hæmoglobin being 7·0 grammes *per centum* in Case 52, while the level in Case 28 was 9·7 grammes *per centum*. In comparison, in Cases 9, 14, 18 and 24 the cord hæmoglobin levels were 12·5, 15·0, 12·7 and 14·6 grammes *per centum* respectively. In Case 24 the hæmoglobin level did not fall below normal, but in the other three it did, there being a fall to 6·2 grammes *per centum* in Case 18. From these figures there seems to be little relationship between the severity of the anæmia and the severity of the original disease.

The time at which the umbilical cord is severed in relation to the infant's birth might be thought to have some bearing. In 10 infants the cord was not severed until it had ceased pulsating. Of these, eight developed anæmia with hæmoglobin levels of mostly between seven and eight grammes *per centum*. It thus could not be suspected that severing the cord immediately or waiting till it ceased pulsating had any influence on the eventual anæmia.

The size of the exchange and the number of exchanges in an individual patient should have some bearing, as the larger the exchange, the less the number of original cells to be subsequently hæmolysed. In the initial stages of the

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 13 to 13, 1956.

Table I.

Showing the Essential Clinical Features and Details of Each Patient.

Case Number.	Cord Tied.	Indications for Exchange Transfusion.	Capillary Hæmoglobin Prior to Exchange (Grammes *per Centum*.)	Exchange Transfusion. (Cubic Centimetres.)			Capillary Hæmoglobin Levels After Exchange Transfusion. (Grammes *per Centum*.)																Duration of Breast Feeding. (Weeks.)	Weight. (Pounds.)			Motor Development.			
				In.	Out.	Balance.	Days.							Weeks.															
							1	2	3	4	5	6	7	2	4	6	8	10	12	14	16	18	20		Birth.	16 Weeks.	One Year.	Head Erect. (Weeks.)	Sitting. (Weeks.)	Pulling Up. (Weeks.)	Walking. One Hand Held. (Weeks.)
1	After pulsation ceased.	Previous sibling died of kernicterus on fourth day.	14·0	470	460	+10	—	—	15·0	—	—	—	13·0	—	9·0	9·0	9·5	9·0	9·8	12·0	—	—	—	7	7½	14	23	12	30	40	52
2	After pulsation ceased.	Jaundice within 12 hours.	16·5	450	470	−20	—	8·5	•	—	—	—	14·5	14·5	7·5	10·5	—	—	—	—	—	—	—	8	7½	13	24	16	32	44	60
4	After pulsation ceased.	Capillary hæmoglobin at birth, 17·0 grammes *per centum*.	17·0	490	505	−15	—	18·5	—	—	—	—	18·0	—	12·5	11·5	11·5	—	13·0	—	—	—	—	10	7½	12½	21	12	28	37	52
9	After pulsation ceased.	Cord hæmoglobin, 12·5 grammes *per centum*.	13·5	500	520	−20	—	11·2	—	—	—	—	10·5	8·5	8·5	9·0	10·0	10·0	11·0	—	—	—	—	28	8	14½	23½	12	32	41	51
10	After pulsation ceased.	Cord hæmoglobin, 11·0 grammes *per centum*.	13·0	420	420	0	—	—	—	14·5	—	—	11·0	9·5	8·5	—	9·0	—	11·5	—	—	—	—	0	8	15½	24½	12	30	32	50
11	After pulsation ceased.	Cord hæmoglobin, 11·0 grammes *per centum*.	14·0	520	520	0	—	—	—	9·0	•	—	15·0	—	7·5	—	7·0	—	—	—	—	—	11·9	2	7	15½	29	16	30	52	54
13[1]	After pulsation ceased.	Jaundice within 12 hours.	11·5	600	620	−20	—	16·0	†	—	—	—	16·0	13·0	11·0	—	10·0	11·0	—	—	—	—	—	10	6½	13	20½	14	34	47	52
14[2]	Immediately.	Cord hæmoglobin, 15·0 grammes *per centum*.	16·0	660	700	−40	12·0	—	—	—	—	—	12·0	—	9·0	7·0	—	10·0	10·5	—	—	—	—	32	7½	14	20½	9	33	50	54
17	Immediately.	Cord hæmoglobin, 9·0 grammes *per centum*.	8·5	400	420	−20	11·0	—	—	9·0	—	—	8·0	8·5	8·5	10·2	—	—	—	—	—	—	—	38	6½	14½	22	12	30	38	52
18	Immediately.	Cord hæmoglobin, 12·7 grammes *per centum*.	14·0	620	660	−40	12·8	—	—	12·0	—	—	11·2	—	—	6·2	—	7·3	—	—	10·4	—	—	36	7½	14	26	16	28	40	50
24	Immediately.	Cord hæmoglobin, 14·6 grammes *per centum*.	19·0	505	525	−20	—	—	18·0	—	—	—	—	13·4	—	13·0	—	—	—	—	—	—	—	5	9	16½	29½	16	29	40	51
26	After pulsation ceased.	Jaundice within 12 hours.	22·0	500	520	−20	—	11·0	—	—	—	—	14·0	—	7·6	—	9·0	—	—	—	10·4	—	—	16	7½	12½	24	16	28	40	52
27	Immediately.	Jaundice within 12 hours.	11·3	580	620	−40	12·0	†	—	9·8	—	—	9·5	7·5	6·0	7·6	—	8·7	10·8	—	—	—	—	20	6½	13	23½	13	30	42	52
28	Immediately.	Cord hæmoglobin, 4·6 grammes *per centum*.	6·4	600	640	−40	12·3	—	—	—	—	—	—	11·9	—	9·7	—	10·9	—	—	—	—	—	16	7½	14	23½	16	28	44	52
30	Immediately.	Cord hæmoglobin, 8·8 grammes *per centum*.	12·8	570	580	−10	—	—	—	17·0	—	—	—	16·2	14·4	—	13·6	—	—	14·4	—	—	—	8	7½	11½	23½	16	32	43	56
33	Immediately.	Cord hæmoglobin, 11·7 grammes *per centum*.	12·0	580	600	−20	—	—	—	11·1	—	—	—	10·1	6·5	6·0	6·0	7·6	9·5	—	9·6	—	10·0	6	6½	15½	26	16	30	42	54
37[3]	Immediately.	Cord hæmoglobin, 9·3 grammes *per centum*.	15·4	620	660	−40	—	—	9·5	—	—	—	9·3	—	7·3	6·0	7·0	8·8	9·4	10·6	—	—	—	11	7	14	23	16	28	40	52
38	After pulsation ceased.	Reticulocytes, 10·6 *per centum* of red cells. Serum bilirubin at one hour, 3·4 milligrammes *per centum*.	18·0	500	500	0	—	—	—	11·5	—	—	11·8	—	—	—	8·0	7·2	8·5	—	10·8	—	—	20	7	12½	20	16	28	41	52
39	Immediately.	Cord hæmoglobin, 11·0 grammes *per centum*.	16·2	580	600	−20	—	—	10·6	—	—	—	—	8·3	6·0	7·8	9·0	9·0	9·2	—	10·2	—	—	40	7	14½	22	16	27	40	52
41	Immediately.	Cord hæmoglobin, 7·2 grammes *per centum*.	9·2	540	580	−40	—	10·9	—	—	—	—	8·8	7·6	8·3	10·1	—	—	—	—	—	—	—	28	7	14	22	16	28	40	52
43	Immediately.	Cord hæmoglobin, 11·4 grammes *per centum*.	12·0	600	620	−20	13·7	—	—	14·2	—	—	—	11·5	—	11·5	11·0	—	—	—	—	—	—	40	7½	13½	—	16	32	40	—
45	After pulsation ceased.	Serum bilirubin at 26 hours, 18·0 milligrammes *per centum*.	15·0	670	700	−30	—	12·5	—	—	—	—	11·0	10·5	7·5	9·5	10·5	11·5	—	—	—	—	—	4	7½	14	—	12	30	40	—
47	Immediately.	Cord hæmoglobin, 10·2 grammes *per centum*.	13·0	740	760	−20	12·0	†	—	9·5	—	—	7·2	7·4	8·0	8·5	10·0	10·0	—	—	—	—	—	6	6½	14½	—	12	30	—	—
50	Immediately.	Jaundice within 12 hours.	13·0	695	705	−10	14·0	—	—	15·0	—	—	16·0	15·0	14·5	12·2	—	—	—	—	—	—	—	4	6	12	—	10	28	—	—
51	Immediately.	Nucleated red cells, 26·0 *per centum* of all nucleated blood cells.	19·0	600	620	−20	14·0	—	—	13·5	—	—	15·0	—	9·5	—	9·1	—	10·1	—	—	—	—	8	6	14½	—	12	30	—	—
52	Immediately.	Cord hæmoglobin, 4·0 grammes *per centum*.	6·0	660	700	−40	15·0	—	—	—	—	—	13·5	11·0	7·0	9·1	8·3	8·9	11·1	—	—	—	—	28	5½	12½	—	16	28	—	—
54	Immediately.	Cord hæmoglobin, 7·2 grammes *per centum*.	9·8	620	640	−20	15·5	—	—	15·5	—	—	14·2	11·8	9·5	8·5	9·0	8·8	9·5	—	12·0	—	—	0	6½	13	—	17	28	—	—
55	Immediately.	Cord hæmoglobin, 4·5 grammes *per centum*.	7·5	800	840	−40	13·1	—	—	11·2	—	—	10·0	—	8·5	8·8	10·5	—	—	—	—	—	—	16	8	14	—	16	—	—	—

[1] Mother Rh-positive. Sensitized to c. [2] Sibling of Case 1. [3] Sibling of Case 2. • Transfusion. † Repeat exchange.

study much smaller exchanges were carried out (Cases 1, 2, 4, 9, 10, 11). However, there was no greater incidence or severity of anæmia among these patients than among those who received a greater volume of exchange at a later period.

It was the procedure in this series to withdraw more blood than was injected at the commencement of the exchange. When the exchange was finished, further blood was withdrawn, if necessary, to reduce the venous pressure in the umbilical vein to eight centimetres of blood. It would be expected that the larger the negative balance of blood existing at the end of an exchange transfusion, the more likely it would be for anæmia to develop. Study of Table I shows, however, that there is no such tendency.

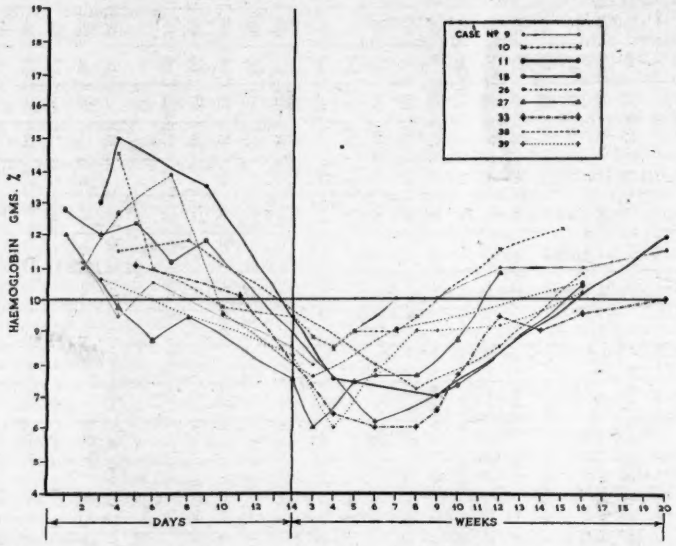

FIGURE I.

Typical changes in nine patients of the series.

The level of capillary hæmoglobin attained immediately after exchange may be of some importance. Of those patients whose hæmoglobin levels subsequent to exchange transfusion were 16 grammes *per centum* or more (Cases 4, 13, 24 and 54) only one (Case 54) subsequently developed anæmia. For this reason the patients most recently treated, none of whom are included in the study, have had exchanges in which packed red cells were used as far as

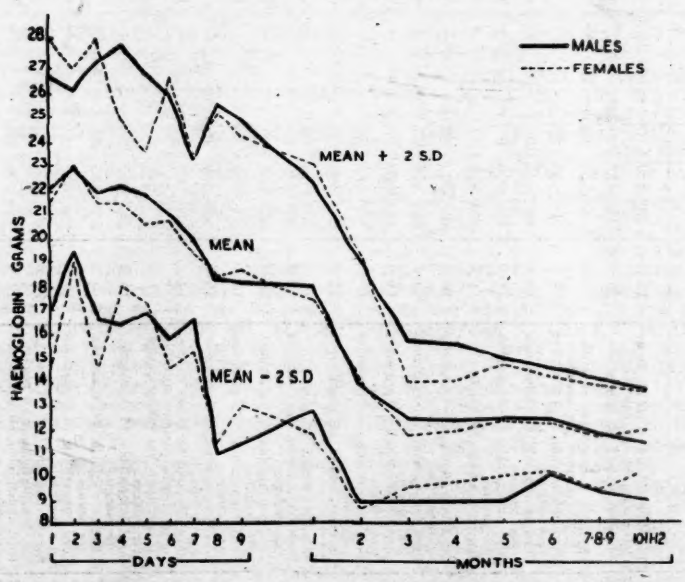

FIGURE II.

possible. It would be wise, however, to sound a word of warning with regard to the use of packed red cells in large exchange transfusions, as a considerable degree of polycythæmia could be brought about with its attendant dangers of vascular thrombosis. The use of packed red cells was originally proposed by Wiener and Wexler (1951), but they used only a small volume of 120 to 150 millilitres. It is the practice at present to use packed cells for about one-third of the exchange transfusion.

The customary procedure has been to give small transfusions to infants whose hæmoglobin content falls to certain levels after exchange transfusion. Mollison, Mourant and Race (1952) recommend this if the hæmoglobin content falls below 7·5 grammes *per centum* after

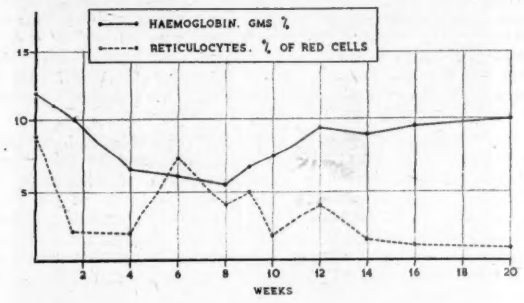

FIGURE III.
Changes in hæmoglobin levels and reticulocytes when anæmia has been severe.

the first three to four weeks of life only. Walker and Neligan (1955) recommend transfusion at a level of less than 8·5 grammes *per centum*. However, Diamond and Allen (1952) did not recommend transfusions if the infants were gaining weight and eating and sleeping well, even if the hæmoglobin level fell to six grammes *per centum*. They thought that transfusions tended to delay rather than

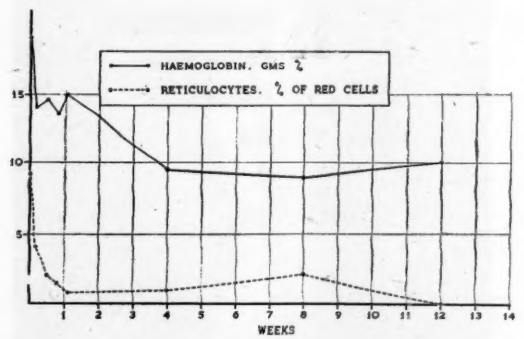

FIGURE IV.
Changes in hæmoglobin levels and reticulocytes when anæmia has been mild.

speed the ultimate recovery. It is conceivable that small transfusions will delay activity of the bone marrow and prevent spontaneous recovery. It is a common experience that a small transfusion of 100 millilitres of whole blood will raise the hæmoglobin level by three grammes *per centum* which is followed in a few weeks by a fall to the pretransfusion level. This is illustrated in Figure V.

I hope it will be agreed that there is no evidence in this series of cases that any harm results from allowing regeneration of the infants' bone marrow to cause spontaneous rise in the hæmoglobin level to normal. Pierce (1955) states that there is little or no evidence that anæmia *per se* contributes to retarded development. He quotes three patients with pure red cell anæmia, who are alert and normal in growth and development, with a hæmoglobin level of less than seven grammes *per centum* throughout their lives.

Apart from the fact that the temporary anæmia of these infants does not interfere with growth or mental development, would simple transfusions cause any harm? It is probable that small transfusions will delay active regeneration of the bone marrow, as already mentioned. Unless the transfusion is given by a scalp vein, a cut down on the long saphenous vein is necessary with the ever-present danger of infection of the wound. Careful cross-matching will prevent transfusion reactions, but accidents will always happen. The main dangers of transfusion are mistakes in labelling and undetectable infection of the transfused blood (Walsh, 1956).

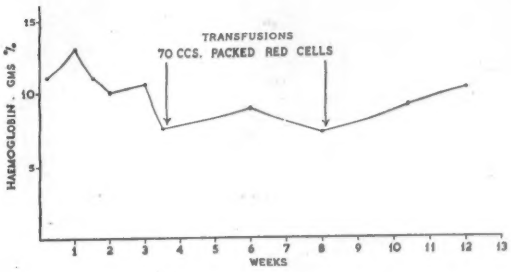

FIGURE V.
Illustrating the temporary rise in hæmoglobin level after a transfusion, with subsequent fall and attainment of a normal level in the same time as when no transfusions have been given.

Summary.

A study in 22 infants of the anæmia which often follows exchange transfusion in hæmolytic disease of the newborn is presented. The hæmoglobin level of some infants fell as low as six grammes *per centum*. Two simple transfusions only were given. Careful observation could not detect any physical or mental retardation in these infants. The hæmoglobin level spontaneously rose to normal at some time in the first five months of life. The cause of the anæmia could not be related to the initial severity of the disease as judged by the cord hæmoglobin levels, to early or late tying of the umbilical cord, to the volume of the exchange transfusion or to the size of the negative balance of the procedure. It is thought that the higher the hæmoglobin level at the end of the exchange transfusion, the less likely is it that anæmia will develop, and that the use of a proportion of packed red cells in the transfusion may be recommended. It is thought that small simple transfusions for anæmia following exchange transfusions are unnecessary and may be dangerous.

Acknowledgements.

I am indebted to the obstetric and pædiatric members of the staff of Saint Margaret's Hospital for Women for allowing me to treat and follow up these patients. I am also indebted to Dr. Margaret Collins, formerly pathologist at this hospital, without whose help the study would not have been possible.

References.

ASHBY, W. (1919), "The Determination of the Life of the Transfused Blood Corpuscles in Man", *J. Exper. Med.*, 29: 267.

DIAMOND, L. K., and ALLEN, F. H. (1952), "Erythroblastosis Fœtalis", *Pediatrics*, 10: 337.

HYMAN, C. B., and STURGEON, P. (1955), "Observations on the Convalescent Phase of Erythroblastosis Fetalis", *Pediatrics*, 16: 15.

LEVINE, P., VOGEL, P., and ROSENFIELD, R. E. (1953), "Hemolytic Disease of the Newborn", "Advances in Pediatrics", 6: 97.

MOLLISON, P. L., and CUTBUSH, M. (1949), "Hæmolytic Disease of the Newborn, Criteria of Severity", *Brit. M. J.*, 1 : 123.

MOLLISON, P. L., MOURANT, A. E., and RACE, R. R. (1952), "The Rh Blood Groups and their Clinical Effects", Medical Research Council Memorandum, Number 27, page 40.

PIERCE, M. (1955), "The Pale Child", *Pediatric Clinics of North America*, 2 : 427.

WALKER, W., and NELIGAN, G. A. (1955), "Exchange Transfusion in Hæmolytic Disease of the Newborn", *Brit. M. J.*, 1 : 681.

WALSH, R. J., ARNOLD, B. J., LANCASTER, H. O., COOTE, M. A., and COTTER, H. (1953), "A Study of Hæmoglobin Values in New South Wales", National Health and Medical Research Council, Special Report Series Number 5, Canberra.

WALSH, R. J. (1956), personal communication.

WIENER, A. S., and WEXLER, L. B. (1951), "Modification of Technic of Treating Erythroblastosis Fetalis by Exchange Transfusion", *Pediatrics*, 8 : 117.

FEBRILE CONVULSIONS IN INFANCY AND CHILDHOOD.[1]

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A FEBRILE CONVULSION in a child is a very dramatic occurrence which terrifies both the patient and his family. Once the acute episode is over, speculation begins. "Will this occur again?" "Will the infant become an epileptic?" These are important questions, and it is small wonder that pædiatricians the world over have sought a definite answer.

Writers in medical literature are sharply divided on the ultimate prognosis of febrile convulsions. Peterman (1952), of Milwaukee, who has spent thirty years studying epilepsy in childhood, lays great importance on the serious prognosis in a large percentage of cases. He has emphasized that it is the general practitioner who most frequently observes the initial febrile convulsion, and that he would do well to consider this symptom as one of the most serious in childhood.

Livingston, Bridge and Kadji (1947) report 94 cases, in which the first convulsion was attributed to fever. The patients were followed for a period of fourteen years. From their series the authors report that the prognosis for recovery is good for patients with febrile convulsions, and better for those having few recurrences and those whose near relatives give a similar history.

Faxen (1953) and Herlitz (1954) have stated that the prognosis of febrile convulsions is good.

Patrick and Levy (1924) concluded that infantile convulsions increased the patients' chance of subsequent epilepsy five times. Thom (1942) calculated that the chances were increased 12 times. These sombre views are in definite contrast with our experience in Sydney, and it was felt that the present investigation might help to elucidate the frequency and prognosis of febrile convulsions in infancy.

Definition.

We have found it difficult to define a febrile convulsion. For the purposes of this study, a convulsion has been defined as "a temporary loss or impairment of consciousness with involuntary muscle movement or loss of postural tone associated with various autonomic upsets". Evidence for the febrile nature of these convulsions has included, naturally, fever, although we realize that the first recorded rise in temperature must often of necessity have been noted after the convulsive episode. Other evidence has been used to confirm the febrile nature of these convulsions—this includes evidence of diseases such as tonsillitis, otitis, enteritis *et cetera*, leucocytosis, raised sedimentation rate *et cetera*.

In the majority of papers studied the authors have not defined exactly what have been their criteria for the diagnosis of a "febrile convulsion".

We have omitted from this series all forms of convulsions in which there was a known underlying cause (for example, severe birth trauma, agenesis, encephalitis and meningitis, intoxications and hypoglycæmia).

Two studies have been carried out concurrently. A prospective survey was made of those patients with febrile convulsions admitted to the Royal Alexandra Hospital for Children in the year 1953-1954. This series will be the subject of a later report. A retrospective survey was also carried out on patients with "febrile convulsions" admitted to the Royal Alexandra Hospital in the years 1943 to 1945. This retrospective series is the basis of the present report.

Frequency.

It is the custom at the Royal Alexandra Hospital for Children to admit all children with convulsions directly from the casualty ward. The 100 cases studied in the retrospective survey comprised patients admitted over a three-year period, 1943-1945. This was during the later part of World War II; many histories were difficult to trace and thus these figures do not give a true picture of the frequency of febrile convulsions.

During the twelve-month period from November, 1953, to October, 1954, 160 infants were admitted to the Royal Alexandra Hospital for Children with a diagnosis of "febrile convulsions". This is equal to 1·3% of children admitted. W. G. Lennox (1953) quotes Peterman's figures for Johns Hopkins Hospital; in his series febrile convulsions equalled 2·3% of admissions, a number equal to the admissions for rheumatic fever, and double those for tuberculosis.

Age Incidence of First Attack.

Figure I shows the age incidence of the first attack of febrile convulsions. The highest incidence was in the six to twelve months age group—35 cases; 28 patients were aged twelve to eighteen months and 22 eighteen to twenty-four months. After the age of two years febrile convulsions were seldom seen. In our series 97% of the febrile

FIGURE I.

convulsions occurred in the first three years of life. During the first six months of life only one case occurred. In our experience most children who have convulsions in this age group have a history of birth trauma or agenesis. Certainly several cases (not included in this series) were seen; in these there was a definite history of birth trauma, and a convulsion occurred associated with a febrile episode in the first six months of life.

Sex Incidence.

Like most authors, we have found that the incidence of febrile convulsions is somewhat higher in boys (54 cases) than in girls (46 cases). The cause of the fever in these cases can be seen from Table I.

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 13 to 16, 1956.

ILLUSTRATIONS TO THE ARTICLE BY FRIEDA E. PLARRE, M.D., D.D.R.

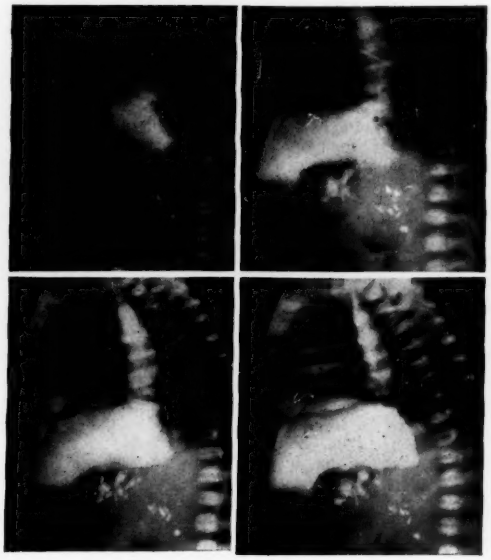


FIGURE IV.

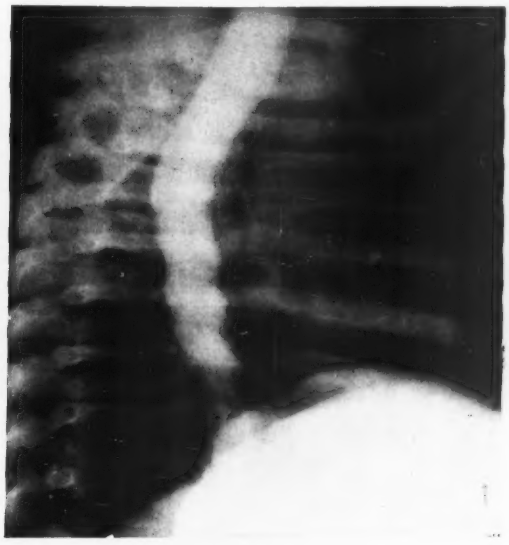
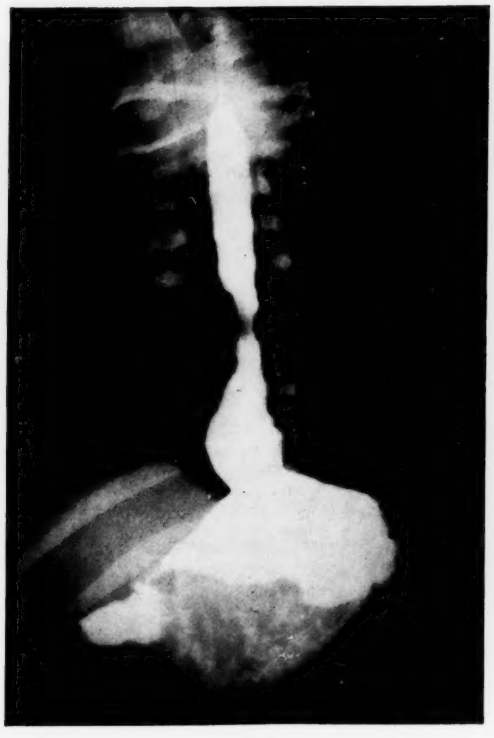


FIGURE V.



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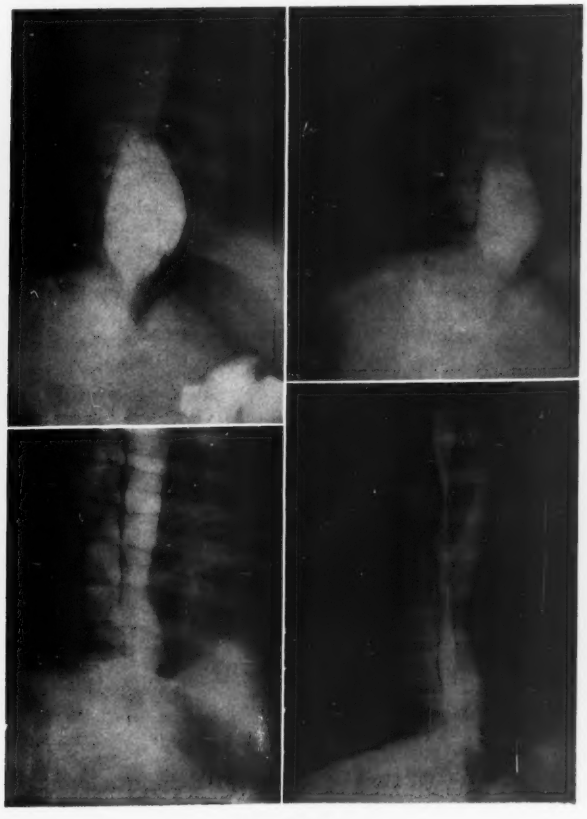
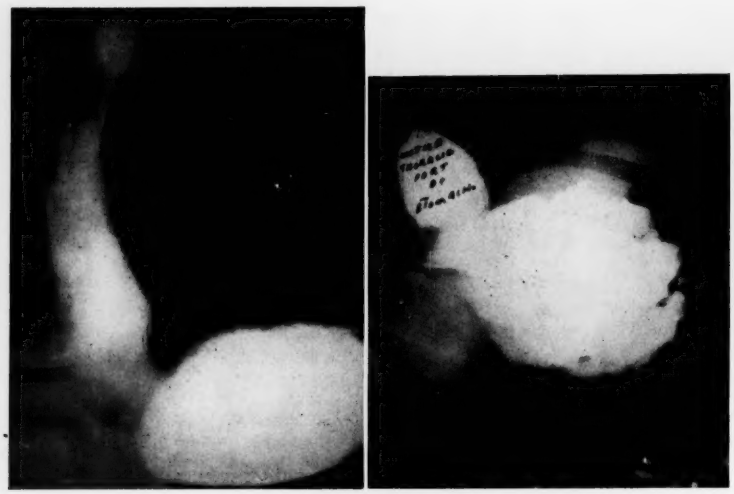


FIGURE VII.

ILLUSTRATIONS TO THE ARTICLE BY FRIEDA E PLARRE, M.D., D.D.R.



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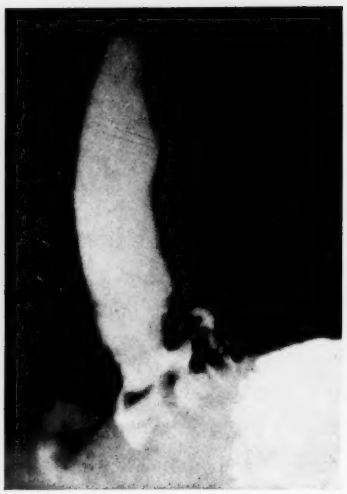

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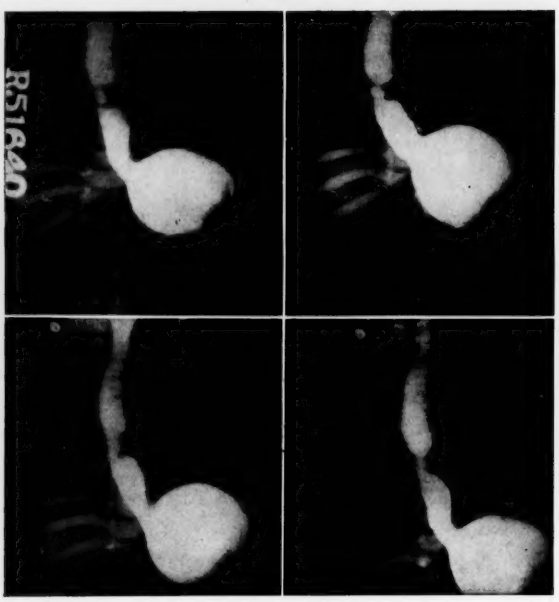


FIGURE X.

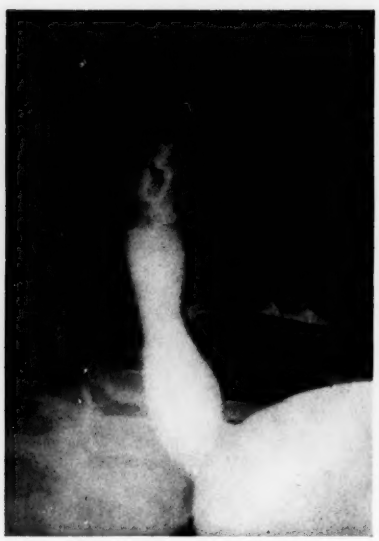
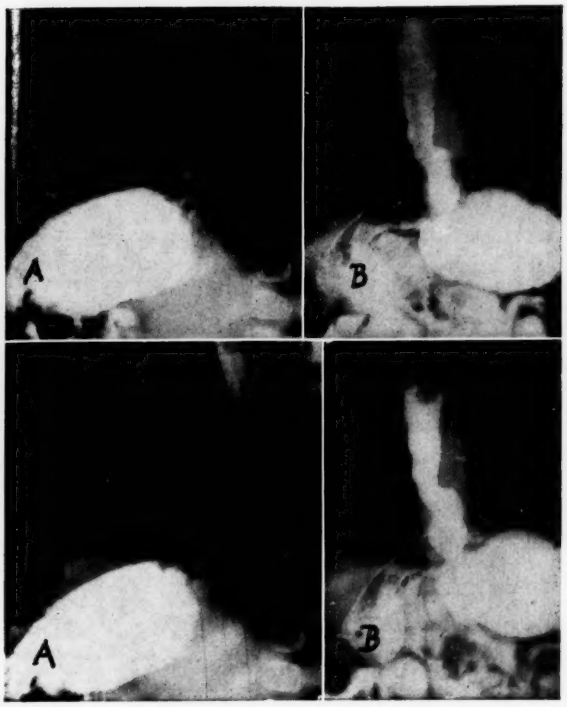


FIGURE XI.

ILLUSTRATIONS TO THE ARTICLE BY FRIEDA E. PLARRE, M.D., D.D.R.



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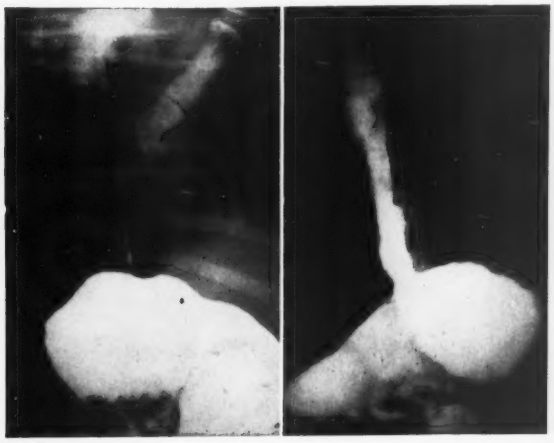

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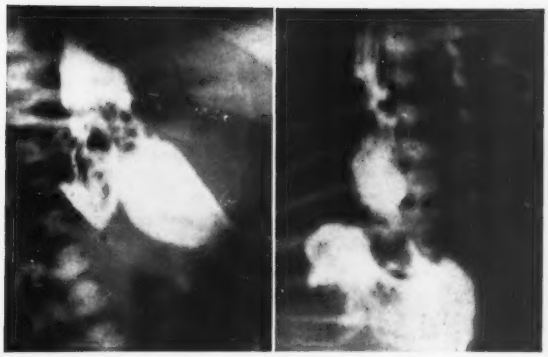

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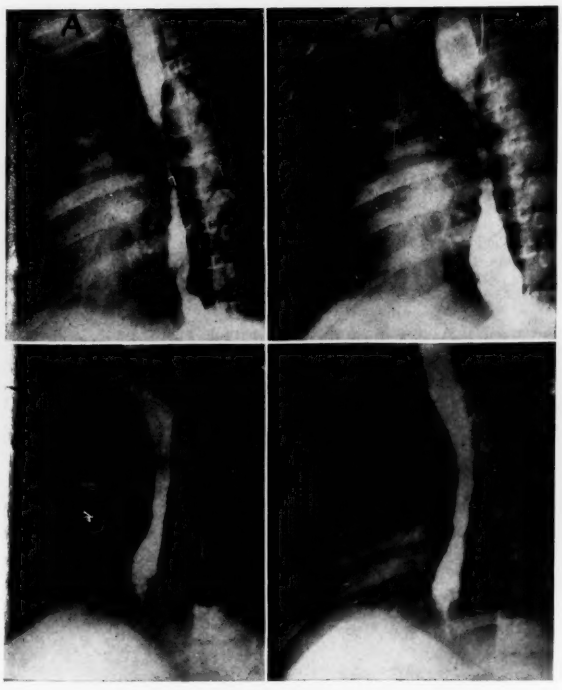

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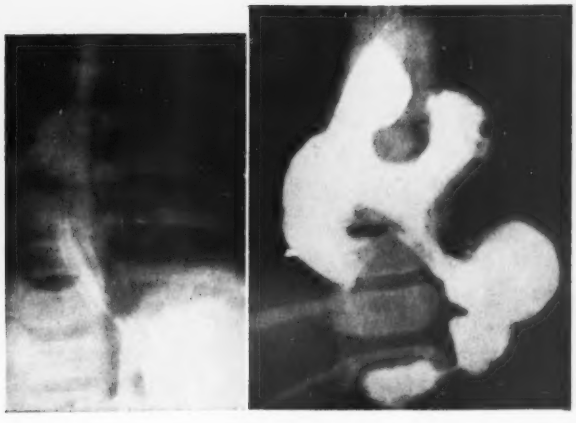

FIGURE XVI.

ILLUSTRATIONS TO THE ARTICLE BY D. C. JACKSON.

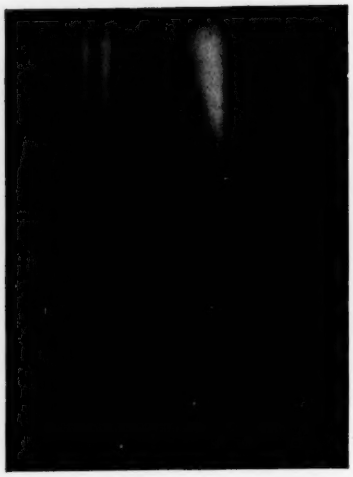

FIGURE V: July 14, 1954.

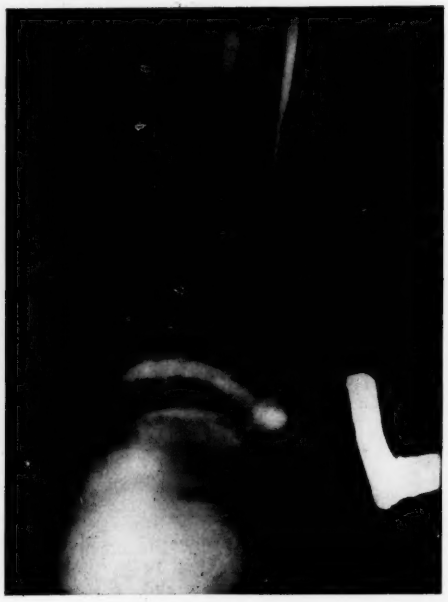

FIGURE VI: September 27, 1954.

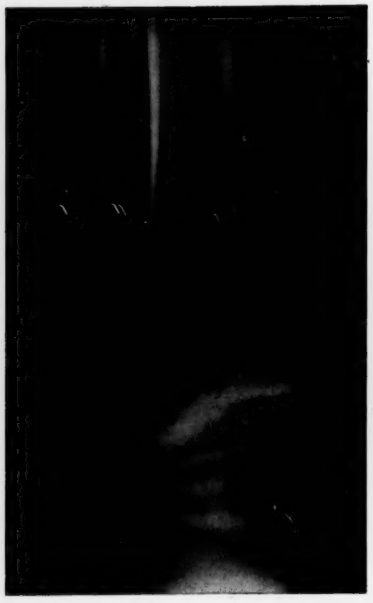

FIGURE VII: October 25, 1954.

FIGURE VIII: November 28, 1954.

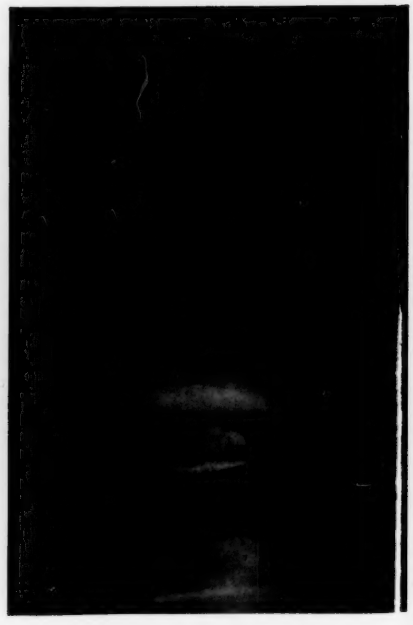

FIGURE IX: March 7, 1956.

Children with acute epidemic diseases are not admitted to the Royal Alexandra Hospital if the illness is diagnosed prior to admission, and consequently the figure of 10% in this series is probably lower than the true incidence in the general child population.

The Mechanisms of Febrile Convulsions.

W. G. Lennox (1953) has attempted to explain why some children respond to a febrile disturbance by a convulsion. He points out that most pædiatricians would affirm that a seizure which accompanies a fever is an innocent symptom much akin to a rigor in an adult.

TABLE I.

Causes of Fever in 100 Cases.

Infection.	Number of Cases.
Tonsillitis	31
Pneumonia and bronchitis	15
Otitis media	13
Upper respiratory tract infection	9
Enteritis	5
Measles, scarlet fever, whooping cough	10
Miscellaneous	5
Unknown	12

Indeed an aphorism of Hippocrates is "a convulsion in a fever is good—for that which accompanies the fever is expelled by the convulsion". Nevertheless, why is it that only an occasional child exhibits a febrile convulsion with an infection? Lennox states that in the absence of experimental evidence to the contrary we must assume that fever and infection acting together induce so-called febrile convulsions.

The risk of seizure increases with the temperature and the seizure usually appears at the ascending curve or at the crest of the temperature.

Wegman (1939) has examined this in experiments on kittens (over five to six weeks old) placed in an electrically heated cage. He demonstrated that whereas full-grown cats very seldom have convulsions, a sudden raising of the temperature will often start convulsions in the young kitten. However, he also found that if the temperature rises slowly convulsions are rare, even if the rise in temperature is very high.

Quite often in our series the histories state that the child "suddenly ran a temperature". But why do so few children have febrile convulsions? After all, the majority, if not all, young patients have had high fevers. Undoubtely, quite apart from the "triggering" action of the febrile disturbance, a most important factor is the underlying predisposition or inherited tendency to seizures.

Prognosis.

In every instance of "febrile convulsions" the important question arises: "Is this a case of incipient epilepsy?" As a corollary to this question, and of obvious practical importance, is the formulation of a group of prognostic features which will help us chose those patients who will continue to have convulsions and become epileptics.

In our retrospective study we have attempted a follow-up of 100 patients admitted to hospital some ten years earlier with the diagnosis of "febrile convulsions".

A number of publications have dealt with this subject in a similar manner and the results are shown in Table II.

It will be seen that the Scandinavian series are the longest, and that they also show the lowest percentage of epilepsy, namely 3% to 5%.

Zellweger's series originated from the University Clinic in Zurich, where undoubtedly many severely ill children are admitted; hence the high percentage of epilepsy (14% of cases of epilepsy, 7% of suspected cases). The same applies to Peterman's (1950) publication.

The follow-up of our patients has been difficult, because the period during which the children were admitted to hospital in their initial convulsion included the war years. Over 80% of these patients had changed their address since the time of admission. However, of the 100 patients covered by this paper, the great majority were examined personally by me; for the remainder either

TABLE II.

Year.	Author.	Number of Cases.	Epilepsy *per Centum.*	Prognosis.
1935	Faxen	238	5·0	Good.
1942	Herlitz	424	3·2	Good.
1948	Zellweger	105	21·0	Bad.
1950	Peterman	128	31·0	Bad.
1953	Livingston	201	3·0	Good.
1954	Friderichsen	282	2·8	Good.
—	Cary	100	6·0	Good.
—	Patrick and Levy	—	—	Bad.

a comprehensive *questionnaire* was adequately answered or an interview was held by a social worker using this *questionnaire*. The results of the follow-up are given in Figure II.

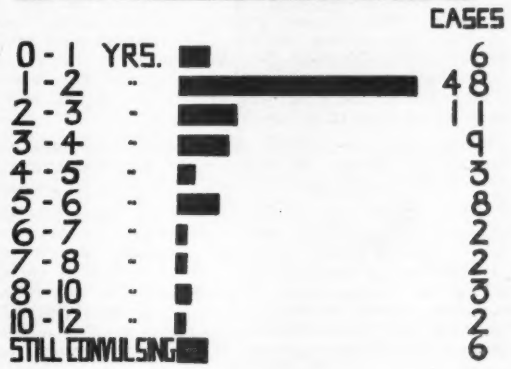

FIGURE II.

It will be seen that 54% of these children had their last convulsion by the age of two years and 85% by the age of six years. Ten years after the initial febrile convulsion, six children were still suffering from convulsions and were regarded as epileptics; five of these were thought to be sufferers from *grand mal* epilepsy and the remaining child had *petit mal*.

Clinical histories of these six patients follow.

CASE I.—B. was a boy. The initial febrile convulsion occurred at two years and four months. It was generalized and lasted more than half an hour. Tonsillitis was the exciting factor. He had one convulsion in the original episode. There is no family history of convulsions. At the age of fifteen years the child is normal physically, and his intelligence is fair.

CASE II.—R., a boy, had the initial convulsion at thirteen months. It was generalized and the duration was less than ten minutes. The cause of the fever was tonsillitis associated with otitis. There is a normal family history. Now at the age of twelve and a half years he is normal physically and is a good scholar.

CASE III.—J., a boy, had the initial convulsion at thirteen months; it was generalized and lasted for twenty minutes. The episode was associated with tonsillitis and otitis. There was a family history of convulsions. Now at the age of thirteen years he is normal physically but slightly backward mentally.

CASE IV.—C., a girl, had the initial febrile convulsion at ten months of age. It was generalized and the duration was more than sixty minutes. The exciting factor was gastro-

enteritis. There is a family history of convulsions. At the age of twelve years this child revealed no abnormality on physical examination, and her intelligence quotient was normal. She is now having right-sided convulsions.

CASE V.—P., a boy, had the initial convulsion at fourteen months; it was generalized and of indefinite duration. There is a family history of convulsions. He is now backward, and a recent electroencephalogram suggests brain damage.

CASE VI.—R., a boy, had an initial episode at twenty-four months associated with pneumonia. The convulsion was generalized and the duration was forty-five minutes. There is no family history of epilepsy. He now has *petit mal*.

All these children were born at full term, and delivery was normal.

In 37 of this series of 100 cases there was in the immediate family a history of either epilepsy or febrile convulsions.

Discussion.

In this survey we have paid particular attention to certain features of the actual convulsive episodes. These were: (*a*) duration of the convulsion; (*b*) type of convulsion (generalized or focal); (*c*) family history; (*d*) the patient's age at the time of the initial episode.

Margaret Lennox (1949) in a retrospective survey of cases of recurrent convulsions, in which the first convulsion was attributed to fever, found that important prognostic features were: (*a*) the severity of the convulsion; (*b*) electroencephalographic changes; (*c*) age at onset (those with a poor prognosis began earlier—one-third of the cases before one year); (*d*) the slightly worse prognosis among females; (*e*) the number of convulsions (it was found that a total of more than three febrile convulsions affected the prognosis adversely); (*f*) a family history, which was important.

Unfortunately, we have no electroencephalographic records for our cases. No suitable machine was available when these children were originally admitted to hospital.

It will be seen from a study of the six cases that progressed to epilepsy that none exhibited many or all of Margaret Lennox's bad prognostic features. Five of the six children were males. Five had their initial episode after the age of one year. All suffered from generalized convulsions, and in four of the six cases the duration of the episode was greater than thirty minutes. Half of these patients had a family history of epilepsy or febrile convulsions.

In contrast, some of the remaining 94 children in this series, who have not progressed to epilepsy, showed many of these signs which Margaret Lennox feels indicate a poor prognosis.

F., a boy, had his initial febrile convulsion at two and a half years. Signs were localized to the right side, and the duration was more than one hour. The family history was negative. He had four similar convulsions before the age of three and a half years. Since then he has been free of convulsions. Now at thirteen years he is a normal healthy boy.

M., a boy, at twelve months of age had a right-sided convulsion associated with tonsillitis. The duration was greater than thirty minutes. There was no family history of convulsions. This was the only episode, and he is now a normal boy of twelve years.

Of the children, 35% experienced their first convulsion before twelve months, but in only 6% of all the cases did the condition go on to epilepsy. In addition, of the 94 cases which did not progress to epilepsy the initial convulsion in 27 was of greater than thirty minutes' duration.

Conclusion.

In this series of 100 cases of febrile convulsions, followed for a period of at least ten years, only six patients are still liable to convulsions, and have been diagnosed as suffering from epilepsy.

The prognosis of febrile convulsions must be considered favourable.

I have found it very difficult, if not impossible, to be dogmatic as to which type of case is liable to progress to epilepsy.

In view of this finding and the overall favourable prognosis of febrile convulsions, I do not consider it justified to trouble the patients with anti-epileptic treatment for several years.

Acknowledgements.

I am indebted to Professor Lorimer Dods for his help and encouragement, to Dr. F. W. Clements for help in the preparation of this paper, and to Miss Grave for her invaluable help in locating many patients.

References.

FAXEN, N. (1953), *"Le prognostic des convulsions de l'enfant"*, *Rev. franç. pédiat.*, 11: 665.

FRIDERICHSEN, C., and MELCHIOR, J. (1954), "Febrile Convulsions in Children: Their Frequency and Prognosis", *Acta pædiat.*, 43, Suppl. 100: 311.

HERLITZ, G., quoted by C. Friderichsen and J. Melchior, *loco citato*.

LENNOX, M. A. (1949), "Febrile Convulsions in Childhood: Their Relationship to Adult Epilepsy", *J. Pediat.*, 35: 427.

LENNOX, W. G. (1953), "Significance of Febrile Convulsions", *Pediatrics*, 11: 341.

LIVINGSTON, S., BRIDGE, E. M., and KADJI, L. (1947), "Febrile Convulsions; Clinical Study with Special Reference to Heredity and Prognosis", *J. Pediat.*, 31: 509.

PATRICK, H. T., and LEVY, D. M. (1924), "Early Convulsions in Epileptics and in Others", *J.A.M.A.*, 821: 375.

PETERMAN, M. G. (1950), "Febrile Convulsions in Children", *J.A.M.A.*, 143: 728.

PETERMAN, M. G. (1952), "Febrile Convulsions", *J. Pediat.*, 41: 537.

THOM, D. A. (1942), "Convulsions of Early Life and Their Relation to Convulsive Disorders and Mental Defect", *Am. J. Psychiat.*, 98: 574.

WEGMAN, M. E. (1939), "Factors Influencing the Relation of Convulsions and Hyperthermia", *J. Pediat.*, 14: 190.

Reports of Cases.

AN UNUSUAL CASE OF AMINOACIDURIA WITH OTHER BIOCHEMICAL ABNORMALITIES.[1]

By D. C. JACKSON,
Brisbane.

IN recent years much attention has been paid to the group of disorders in childhood which are considered to result from defects in reabsorption by the renal tubules, and which are probably congenital in origin.

The accumulating studies have made it clear that there are many possible variations of the reabsorptive deficiencies, and Jackson and Linder (1953) have suggested that a term such as "multiple defects of tubular function" should be applied collectively to this group of disorders.

McCune, Mason and Clarke (1943) made an important contribution to the literature in a communication which included a review of the reports of, or allusions to, rickets accompanied by non-diabetic glycosuria, which had appeared during the previous fifteen years. They concluded that no sharply definable clinical entity could be described, but with regard to nomenclature they pointed out that Fanconi had introduced the concept of tubular renal rickets to account for the pathogenesis of several examples of intractable normoazotæmic, hypophosphatæmic rickets accompanied by chronic acidosis and glycosuria. Although this constellation, as the authors termed it, had been observed before, no well-grounded interpretation had been offered. Attesting the originality and importance of his contribution, Franconi's name was, they considered, properly linked with the complex.

In their Leonard Parsons Memorial Monograph, Bickel, Baar, Astley, Douglas, Finch, Harris, Harvey, Hickmans, Philpott, Smallwood, Smellie and Teale (1952) have not only given a detailed account of the syndrome to which

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 13 to 16, 1956.

they have given the name Lignac-Fanconi disease or cystine storage disease with aminoaciduria and dwarfism, but have also provided an admirable review of many aspects of the symptomatology and investigation of this group of diseases. Their conclusion is that a clearly defined entity—namely, cystine storage disease with aminoaciduria and dwarfism (or Lignac-Faconi disease)—has been isolated from the complex renal rickets group. Bickel and his colleagues consider that the extrarenal origin of this disorder is established.

In a recent paper Fanconi (1954) makes a plea for reasoning less in terms of rigidly defined nosological entities and more in terms of special functions which may be separately upset. In the same paper the author makes this statement:

> The complex reabsorption process, obligatory as well as facultative, may be upset in one of two ways; the reabsorption may be excessive or insufficient. In the case of dextrose and amino-acids, normally completely reabsorbed, there is but one possibility, insufficient reabsorption causing glycosuria and amino-aciduria.

The following case is presented because it shows an unusual and possibly unique combination of symptoms and findings. The child was found to have aminoaciduria and developed hypophosphatæmic rickets, as in the "Fanconi" syndrome, but the third usually accepted concomitant, glycosuria, has been persistently absent. That in itself might not be unusual, and several such cases have been reported (McCune *et alii*, 1943; Boyd and Stearns. 1942), but this child has a hyperglycæmia of diabetic proportions, which responds to insulin. The writer has been unable to find any record of a similar case.

The progress of the investigations has suggested that while the symptoms have been in many ways similar to those of the "Fanconi" group, impaired reabsorptive capacity of the renal tubules, if present at all, has varied during the child's progress under treatment and has possibly been but one manifestation in a complex chain of disordered functions. This suggestion is not incompatible with Fanconi's conception of special functions separately upset as opposed to distinct entities, but implies that the disorders of function may be in themselves variable and that the boundaries of his conception may be considerably widened.

Case History.

The patient, a girl, is now four years old. She is the second of three children; a boy three years older is healthy in all respects, and a younger brother, born in July, 1955, has shown no abnormality to the date of writing. Both parents are in good health, but the mother was said to have cœliac disease in childhood and has had three miscarriages.

The patient was born at term by normal delivery and weighed eight pounds six ounces at birth. She was breast fed to the age of four months, and was then fed on modified cow's milk. She weighed 18 pounds at six months, and 22 pounds at twelve months. She began to walk at twelve months.

Her progress during most of the first year was thus satisfactory, but at the age of ten months she had a short illness described as measles. As the child subsequently developed measles while under observation in hospital, and later *roseola infantum* while under the writer's care at home, the true nature of this illness remains unknown, but from that time onwards she suffered from diarrhœa which proved resistant to treatment. She passed three to five large offensive motions daily, which contained undigested food. There was no vomiting, and there were no urinary symptoms.

She was referred to hospital on account of the diarrhœa, and was admitted on March 3, 1953, being then aged fourteen months. Her diet at that stage consisted chiefly of full-strength cow's milk, of which she drank about 40 ounces (1200 millilitres) daily. Very small amounts of cereal and vegetables were taken reluctantly.

On her admission to hospital her weight was 22 pounds four ounces. She appeared well nourished, but the abdomen was slightly distended and was resistant to palpation. The anterior fontanelle was widely open, but there was no other obvious abnormality.

During the initial investigations she was kept on a normal diet; the stools, of which she passed five or six each day, were pale yellow, usually watery but sometimes pasty, and contained scraps of undigested food. Her fluid intake was 35 to 45 ounces (1050 to 1350 millilitres) daily, and urine was passed nine or 10 times in twenty-four hours. The volume of the fluid output was not measured.

The investigations carried out are shown in Table I.

TABLE I.

Investigation.	Date.	Findings.
Hæmoglobin value	3.3.53 17.4.53 28.4.53	67% (9·4 grammes). 75% (10·5 grammes). 79% (11·2 grammes).
Serum protein content.	4.3.53	7·1 grammes per 100 millilitres of serum.
Blood sedimentation rate.	20.3.53	4·0 millimetres in one hour.
Urine (microscopy)	3.3.53	An occasional pus cell and red blood cell; few uric acid crystals. No casts seen.
Fæces	5.3.53	Trypsin present; no fat globules, ova or cysts; no pathogenic organisms cultured on selective media.
Mantoux test ..	20.3.53 17.4.53	A positive result with one in 1000 old tuberculin. A positive result with one in 1000 old tuberculin. (These results were subsequently considered to be false.)
Gastric lavage *et cetera*.	—	No *Mycobacterium tuberculosis* seen in smear of deposit of gastric lavage. Culture result negative. No *Mycobacterium tuberculosis* seen in fæces.
X-ray examination of chest.	19.3.53	Some slight increase in markings at base of right lung.
X-ray examination of abdomen.	19.3.53	Gas shadows suggestive of slightly distended bowel in left upper quadrant.
X-ray examination of bones.	19.3.53	Wrists, femur, tibia, fibula and humerus normal.

It was decided that the patient's condition chiefly suggested early cœliac disease with diarrhœa starting at the age of ten months and after the introduction of solid foods, with stationary weight, with a distended abdomen and with delayed ossification at the fontanelle; and so a fat analysis on a five-day specimen of fæces was carried out. When the collection was complete, a gluten-free diet was introduced, and the child's condition began to improve. She gained weight, increasing from 19 pounds nine ounces to 23 pounds six ounces between April 15 and May 14, her appetite and disposition improved, and the stools became semi-formed.

The report on the fat analysis was as follows:

Total fat	35·64% by weight of dried fæces.
Neutral fat and free fatty acids	19·8% by weight of dried fæces.
Free fatty acids	5·68% by weight of dried fæces.
Free fatty acids as scraps	15·84% by weight of dried fæces.
Neutral fat (unsplit fat)	14·12% by weight of dried fæces.
Split fat	21·52% by weight of dried fæces.

This was misinterpreted, the unsplit fat being taken as 14% of the total fat, whereas it was really about 40%, and in this error the diagnosis of cœliac disease was made and seemingly confirmed by the response to the gluten-free diet.

She was discharged from hospital on May 23, 1953, but after about a week at home she suffered a relapse. It was discovered that the parents had been sold gluten instead

of gluten-free wheat starch, and this seemed the obvious cause. Attempts at home to reinstitute the correct diet were unsuccessful, and she was readmitted to hospital on June 11, 1953.

Her weight was 20 pounds 14 ounces, and the anterior fontanelle was still widely open. In all other respects her condition remained unchanged.

No investigations of any consequence were carried out during this admission. Again she seemed to respond to the gluten-free diet, became more cheerful and regained her appetite, and the stools became less frequent and were reported as normal by July 20. They were passed once or twice daily. She gained weight and was discharged from hospital on July 30, weighing 22 pounds.

For the next two months a further attempt was made to treat her at home. The improvement in the stools was not maintained and she passed two or three large watery stools daily. Her appetite was very capricious and she slowly lost weight. She was irritable most of the time, and sometimes the parents thought she was weak in the legs and she would not stand up. It was during this time that the parents began to notice her increasing thirst.

She was readmitted to hospital on October 5, 1953, for further investigation, and, the mistake in the interpretation of the fat analysis findings being discovered, the diagnosis was abandoned. The gluten-free diet was continued, as the ward staff were sure the stools were worse when it was not used.

The child had changed very little in appearance, and the anterior fontanelle (she was now twenty-one months old) was still widely open. She was moody, but always ready to walk, and her temper improved when she was allowed out of bed. She was therefore fully ambulant during her time in hospital. Her mental progress seemed normal for her age, but she had lost weight and now weighed 19 pounds 15 ounces.

Her weight remained very constant until her discharge from hospital nearly four months later, when she weighed 20 pounds seven ounces. Her appetite was capricious, but her thirst was remarkable, and she haunted the ward kitchen, soliciting drinks from all who passed. She drank 60 to 70 ounces (1800 to 2100 millilitres) per day and her urinary output was 20 to 30 ounces (600 to 900 millilitres). The balance was probably lost in the stools, which now remained very large and very fluid.

It was now realized that the child presented a metabolic problem much more involved than had been at first suspected, growth having been at a standstill for about nine months.

The following account of the investigations sets them out in approximately the order in which they were made. The principal findings are summarized in Table II.

A routine estimation of hæmoglobin value on her admission to hospital showed no change from previous results. The occurrence of albumin and casts in the urine was now, however, obvious; all specimens examined contained casts, and albumin was present in most. There was no sugar at any time, nor were there any ketone bodies.

The Mantoux test gave negative results (the previous results were considered false), and an examination of a fæcal smear showed no abnormality. The serum protein content was 7·9 grammes per 100 millilitres.

Because of the persisting slight abdominal distension, an X-ray examination was made after a barium meal, the report being as follows:

> The swallow reveals considerable dilatation of the œsophagus. Barium enters stomach freely, but during crying, and particularly in expiration, there is a large reflux of barium from stomach to œsophagus. The stomach is considerably dilated for the age. There is no obstruction and no sign of hernia. The small and large bowels appear normal.

This was an unexpected finding, but neither then nor at any subsequent stage did the child show any symptoms referable to it.

X-ray examination of the wrists and the lower ends of the tibiæ showed no evidence of rickets and no other abnormality.

On November 13, 1953, a glucose tolerance test was carried out after the administration of 30 grammes of glucose by mouth. The result was: fasting blood sugar content, 109 milligrammes per 100 millilitres; half an hour after glucose, 336 milligrammes per 100 millilitres; one hour, 306 milligrammes per 100 millilitres; two hours, 231 milligrammes per 100 millilitres. The urine remained sugar-free throughout. The results of this and subsequent tests are shown as graphs in Figures I to III.

TABLE II.

Showing Findings Between October, 1953, and February, 1954.

Investigation.	Findings.
Urine	Casts in all specimens. Usually albumin. No sugar. Specific gravity, 1000 to 1010.
Blood urea content ..	Maximum, 111 milligrammes *per centum*, December, 1953. Minimum, 60 milligrammes *per centum*, January, 1954.
Serum calcium content	9·5 milligrammes *per centum*.
Phosphorus serum content.	2·4 milligrammes *per centum*.
Fæces, fat content ..	11·5 grammes per day (normal 4·0, average 2·0 grammes).
Blood sugar content (30 grammes glucose).	Fasting—0·109 milligramme *per centum*. After half an hour—0·336 milligramme *per centum*. After one hour—0·306 milligramme *per centum*. After two hours—0·215 milligramme *per centum*.
Chromatogram (urine) ...	Leucine, threonine, serine, glycine and cystine detected. Combined concentrations of leucine, threonine, serine and glycine approximately 40 milligrammes per 100 millilitres. Cystine concentration approximately 300 milligrammes per 100 millilitres). (Normal, 0 to 10.)
Electrophoretic pattern	Albumin, normal. α_1 globulin slightly increased. α_2 globulin much increased. β and γ globulin increased.

When this result was obtained, treatment with crystalline insulin, two units twice daily, was begun and a slight improvement in the child's appetite and general demeanour was noticed. A further glucose tolerance test was carried out on December 3, 1953, while the child was receiving insulin. The results were: fasting blood sugar content, 127 milligrammes per 100 millilitres; half-hour, 191 milligrammes per 100 millilitres; one hour, 221 milligrammes per 100 millilitres; two hours, 186 milligrammes per 100 millilitres. The urine was again sugar-free throughout the test.

This showed that the hyperglycæmia was responsive to insulin, but that the blood-sugar level was still rising above the normal renal threshold without producing glycosuria. Routine ward tests for glycosuria carried out several times daily still gave negative results, and as there seemed a risk of producing hypoglycæmia the insulin dosage was maintained at two units twice daily.

Two further glucose tolerance tests were done with the following results:

> January 12, 1954 (with insulin): fasting, 129 milligrammes per 100 millilitres; half hour, 166 milligrammes per 100 millilitres; one hour, 166 milligrammes per 100 millilitres; two hours, 152 milligrammes per 100 millilitres. All urine specimens were sugar-free.
>
> January 28, 1954 (without insulin): fasting, 105 milligrammes per 100 millilitres; half hour, 241 milligrammes per 100 millilitres; one hour, 241 milligrammes per 100 millilitres; two hours, 196 milligrammes per 100 millilitres. All urine specimens were sugar-free.

These confirmed the previous observation of hyperglycæmia, unaccompanied by glycosuria and sensitive to insulin.

The results of further investigations carried out at this stage are shown in Table III.

Thus the composite picture provided by the observations and investigations to date was that of a child who was not growing, and who had chronic diarrhœa which had seemed to respond to a gluten-free diet and was accompanied by

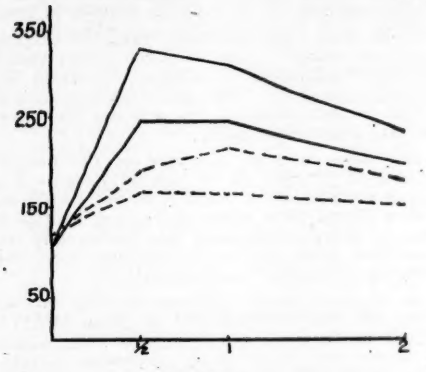

FIGURE I.

Results during the period November, 1953, to January, 1954. The figures on the abscissa are hours, those on the ordinate milligrammes of sugar per 100 millilitres of blood. Interrupted lines indicate tests made while patient was receiving insulin.

an impaired absorption of fat but not of carbohydrate. In addition she showed signs and symptoms suggestive of the Fanconi syndrome, namely, great thirst with aminoaciduria and hypophosphatæmia. There was no radiological evidence of rickets, but it seemed likely that this condition would

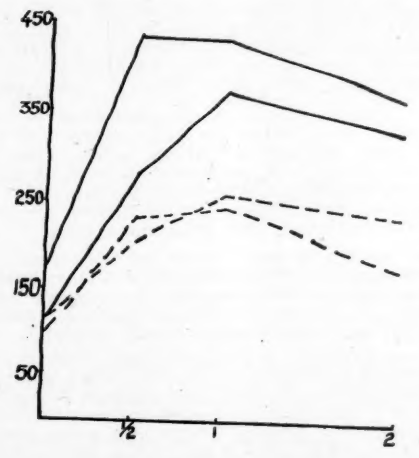

FIGURE II.

Results during the period October, 1954, to November, 1954. The figures on the abscissa are hours, those on the ordinate milligrammes of sugar per 100 millilitres of blood. Interrupted lines indicate tests made while patient was receiving insulin.

appear when she began to grow, and there was a suggestion of retarded ossification in the failure of the fontanelle to close. The absence of glycosuria was, however, puzzling, especially in the presence of hyperglycæmia suggestive of diabetes and sensitive to insulin. Albuminuria and a persistently raised blood urea content were present, and other associated abnormalities were an abnormal electrophoretic pattern and an œsophageal reflux.

The child had now been in hospital for four months, and because of this, further investigation was considered to be unjustified. It was therefore decided to allow her to remain under observation at home, and although her general condition showed no improvement, to withhold all treatment except insulin until rickets appeared or there was further deterioration in her condition.

It was interesting to observe that on her return home her behaviour became more infantile, and she refused to walk or talk, whereas in hospital she had been doing both

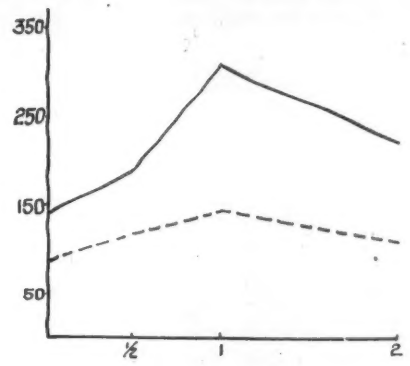

FIGURE III.

Results in July, 1955. The figures on the abscissa are hours, those on the ordinate milligrammes of sugar per 100 millilitres of blood. Interrupted lines indicate tests made while patient was receiving insulin.

quite freely. This phase lasted for about a month, but for the whole of the five months that she now spent at home she was fretful, moody, and difficult to manage. From the physical aspect, these five months were undoubtedly her

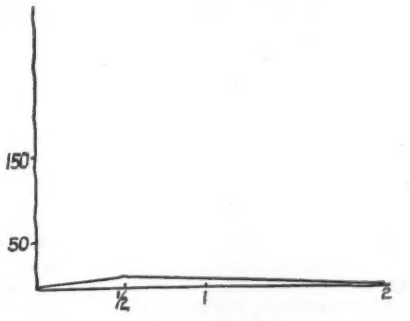

FIGURE IV.

A lævulose tolerance test, March, 1956. The figures on the abscissa are hours, those on the ordinate milligrammes of sugar per 100 millilitres of blood. Interrupted lines indicate tests made while patient was receiving insulin.

worst period. When first examined, a year before, she had appeared reasonably well nourished; but now, although her weight remained about 20 pounds, she seemed to have little subcutaneous fat, the abdomen was prominent, she was pale, and her fair hair seemed lifeless.

She was still having a gluten-free diet, and her parents considered the stools had improved, being much less watery and passed only two or three times daily. Her great thirst remained undiminished.

Some other interesting observations were made by the parents during the ensuing months. She was observed to like salt, and this developed into what they described as a

craving; she would eat it by the handful, consuming half a pound or more per week. Later, cod liver oil was introduced in prophylactic dosage, and this, too, was taken eagerly.

It was also noticed that she had spells of apparent weakness and that she was often unsteady on her legs, and the parents thought she had pain there. Later she actually complained of pain in the legs and refused to walk for that reason.

However, during this same period the fontanelle slowly became smaller, and, despite her capricious appetite, her weight increased from 20 pounds in March to 24 pounds in July. An X-ray examination of wrists and ankles taken on April 23, 1954, was, however, reported as showing no evidence of rickets and the ossification of the epiphyses as being within normal limits.

TABLE III.

Investigation.	Date.	Findings.
Serum phosphorus content.	4. 1.54	2·4 milligrammes per 100 millilitres.
Serum calcium content.	4. 1.54	9·5 milligrammes per 100 millilitres.
Serum acid phosphate content.	12. 1.54	4·4 King-Armstrong units.
Serum alkaline phosphatase content.	12. 1.54	26·0 King-Armstrong units.
Blood urea content	16.12.53	111 milligrammes per 100 millilitres.
	5. 1.54	60 milligrammes per 100 millilitres.
	12. 1.54	77 milligrammes per 100 millilitres.
	9. 2.54	69 milligrammes per 100 millilitres.
Urinary amino acid content.	22.12.53	327 milligrammes of amino-acid nitrogen per day.
	8. 1.54	450 milligrammes of amino-acid nitrogen per day.
	25. 1.54	450 milligrammes of amino-acid nitrogen per day. (Normal, 100 to 150.)
Chromatographic analysis of the urine. (Urine pH 6, centrifuged deposit.)	3. 3.54	Leucine, threonine, serine, glycine and cystine detected. Combined concentrations of leucine, threonine, serine, glycine approximately 40 milligrammes per 100 millilitres. Cystine concentration approximately 300 milligrammes per 100 millilitres. (Normal, 0 to 10.) Some cystine crystals observed.
Urinary phosphates	9. 2.54	3·75 grammes per day (normal, 1 to 5).
Reaction of urine ..	—	Consistently acid.
Faecal fat content[1]	—	11·35 grammes per day. (Normal, 4; average, 2.)
Electrophoretic pattern.	11. 3.54	Protein, 8 grammes *per centum*. Albumin, normal. α_1 globulin, slightly increased. α_2 globulin, much increased. β and γ globulin, increased.
Bone marrow biopsy	9. 2.54	No cystine crystals seen.

[1] After administration of 40 grammes by mouth (Anderson, Fraser *et alii*, 1952).

Towards the end of June she had several attacks of vomiting. She became apathetic and even lost her interest in salt, though she was still very thirsty. In spite of her increase in weight, she now looked worse than ever, and when she could be persuaded to walk, did so unsteadily. The fontanelle was almost closed, but there was splaying of the lower ribs above the distended abdomen, and bowing of both tibiæ was evident just above the ankles.

In this condition she was readmitted to hospital on July 14, 1954.

The principal findings during this admission (July 14 to December 10) and subsequent investigations made while she was at home and during a short admission to hospital in July, 1955, are conveniently grouped in Table IV, which also shows approximately their time-relationship to one another and to the treatment. For simplicity it is proposed to describe her progress by reference to this table, which carries her story to December, 1955.

An X-ray examination made on the day of her admission to hospital confirmed the presence of rickets. This and later films showing the response to treatment are reproduced in Figures V to IX.

The hyperglycæmia continued and remained sensitive to insulin. After the very high readings obtained in November, 1954, the dosage of insulin was increased to five units twice daily. On only one occasion (in July, 1955) was there a very slight reaction of the urine to Benedict's reagent.

It will be seen from the table that the institution of treatment was delayed a little longer. This was because soon after her admission to hospital the child developed measles and some of the initial investigations were delayed. Despite her wasted condition, she was not very ill with the measles, and recovered rapidly.

The treatment adopted consisted of the exhibition of large doses of vitamin *D* as calciferol, and of varying amounts of sodium and potassium citrate. Fifty thousand units of calciferol were given daily, and as the response as shown by X-ray examination was satisfactory, this dose was continued until the serum calcium level showed a high reading, when the dose was halved.

For the administration of citrate the first mixture tried was based on that recommended by Dent (1952), but on account of the low serum potassium level some of the sodium citrate was replaced by potassium citrate. This mixture was not well tolerated, even in smaller dosage, but even in this phase of alkali therapy there was radiological evidence of healing rickets.

In October she had chicken-pox without ill effects, but early in November she contracted an illness of which there was a small outbreak in the ward. She was feverish and vomited for a few days. Her condition was never serious, but citrate therapy was stopped for about a fortnight. Then a mixture, from which citric acid was omitted, and which contained sodium citrate and potassium citrate in the proportions shown, was introduced and given in divided doses. This was well tolerated, and it will be seen that from its introduction the acidosis steadily decreased.

Throughout most of the period covered by the table the blood urea content showed a steady fall. Similar results have been described by others (Bickel *et alii*, 1952). The last reading, however, showed a slight rise. The serum phosphorus levels have varied, being at times rather low.

The behaviour of the serum electrolytes sodium and potassium is hard to correlate with treatment or with the other findings. The sodium level has varied, though remaining about normal, but the potassium level, in spite of a high intake, has remained very low, the value of 15·0 milligrammes per 100 millilitres (3·8 milliequivalents per litre) obtained in December, 1955, being the highest.

In an attempt to find a cause for the persistently low serum potassium level, estimations of urinary sodium and potassium content were made in the hospital laboratory in August, 1954, and by the Department of Physiology in July, 1955. The results obtained were as follows:

> 26.8.54: Volume of urine (24 hours) = 770 ml. Urinary sodium content = 11 mg./100 ml. = 84·7 mg. sodium = 4 mEq/L. Urinary potassium content = 60 mg./100 ml. = 462 mg. potassium = 12 mEq/L.
>
> 28.7.55: Volume of urine (24 hours) = 1130 ml. Urinary sodium content = 4·4 mEq/L. Urinary potassium content = 8·7 mEq/L.

The first result gives a sodium-potassium ratio of 0·3, the second a ratio of 0·5. Both these measurements indicate a relatively high potassium loss with sodium reabsorption.

The only other investigation which need be mentioned at this stage is the search for cystine deposits in the tissues. Bone marrow biopsies had been carried out in February, 1954, and were repeated in December, 1954, and the tissue was examined by the method described by Bickel and Smellie (1952). No cystine crystals were detected on either occasion. Examination of the cornea by slit lamp was impossible at both these times, but was carried out in March, 1956. No cystine deposits were seen.

TABLE IV.

Date.	Blood.		Serum.					Weight. (Pounds.)	X-Ray.	Daily Treatment.		
	Urea. (Milligrammes per Centum.)	Sugar (Range Without Insulin.) (Milligrammes per Centum.)	Calcium. (Milligrammes per Centum.)	Phosphorus. (Milligrammes per Centum.)	Carbon Dioxide. (Per Centum.)	Sodium. (Milligrammes per Centum = Milliequivalents per Litre.)	Potassium. (Milligrammes per Centum = Milliequivalents per Litre.)			Vitamin D. (Units.)	Sodium Citrate. (Grammes.)	Potassium Citrate. (Grammes.)
July, 1954 ..	66	—	—	—	—	340=148	9·5=2·4	24	Rickets.			
August, 1954 ..	—	—	9·0	3·2	—	325=141	11·5=3·0					
September, 1954	—	—	10·3 10·5	5·0 5·5	46 44	—	—		Healing.	50,000	4	6
October, 1954 ..	—	—	10·5	5·0	41 40	305=132	11·5=3·0	26			2	3
November, 1954	57	172–447 114–374	10·6 11·6	5·2 4·5	54	315=137	13·5=3·4			Treatment stopped (illness)		
February, 1955 ..	54	—	12·0	4·6	—	—	13·0=3·3	29				
May, 1955 ..	42	—	11·6	3·6	—	320=139	11·0=2·8	30		50,000	10	8·5
July, 1955 ..	30	141–307	14·0	3·3	61 72 75	310=134·7	9·5=2·4					
December, 1955	48	—	11·5	5·3	56	330=143·5	15·0=3·8	34	Normal.	25,000		

As soon as the child's condition began to improve she was discharged from hospital (on December 10, 1954), and since then has progressed very well, increasing steadily in weight and height and behaving at home in all ways as a normal child of her age. The results of investigations made at various times up to December, 1955, are shown in Table IV, and in the appendix.

She contracted *roseola infantum* in April, 1955, but has had no other illness. Her thirst has continued and she wakes at night asking for water, but there has been no return of her craving for salt. The bowel motions have varied somewhat, usually occurring two or three times daily, and the stools are usually large and watery, though occasionally large and semi-solid. They are always pale and offensive. She has full control of bowels and bladder by day, but has occasional nocturnal enuresis.

About May, 1955, the parents remarked on occasional periorbital swelling accompanied by swelling of the hands and feet. This was occasional and transient and was not observed by the writer until December, 1955, when a slight moulding of the dorsum of the feet from shoe pressure was noticed at one visit.

On March 4, 1956, she was readmitted to hospital for further investigation. She looked very well, and no œdema was apparent. However, within a few days of admission her face appeared thinner, so it may be assumed that slight periorbital swelling had been present. It was interesting to learn from the parents, who had seen her frequently in hospital, that within twenty-four hours of her discharge (on March 22, 1956) the puffiness of the face, hands and feet was again present. There was no albuminuria while she was in hospital, and in contrast to earlier observations the urine was microscopically normal.

The other investigations carried out during this admission were mainly repeats of those already recorded, and these will be enumerated first.

The levels of serum sodium and potassium were virtually unchanged, the sodium content being 315 milligrammes per 100 millilitres (137 milliequivalents per litre), and the potassium 12 milligrammes per 100 millilitres (3·06 milliequivalents per litre). The serum chloride content was 602 milligrammes per 100 millilitres, and the serum carbon dioxide combining power 52 volumes *per centum*.

Blood calcium and phosphorus contents were 13 milligrammes per 100 millilitres and 4·2 milligrammes per 100 millilitres, respectively.

All these were consistent with previous findings, but estimation of the sodium and potassium levels in a twenty-four hour specimen of urine showed (in 1634 millilitres of urine) 5·0 milliequivalents per litre of sodium and 2·5 milliequivalents per litre of potassium (1·85 grammes and 1·6 grammes per twenty-four hours, respectively).

Thus, although the urine volume continued to be very large, there was now sodium excretion in greater quantity than potassium, and the sodium-potassium ratio was 2·0, a complete reversal of former results.

An examination of the urine for amino-acids also showed an interesting change from the findings of earlier tests. There was now no evidence of abnormal amino-acid excretion, either quantitatively or by chromatography.

Of investigations carried out for the first time, slit lamp examination has already been mentioned. An estimation of 17 hydroxycorticosteroids gave a result of less than 1·6 milligrammes per twenty-four hours, which is a low reading for a child of this age. Sugar chromatography showed no sugar of any kind in the urine, and a lævulose tolerance test gave a normal result and was unaccompanied by any reducing substance in the urine.

Finally, in order to obtain a measurement of the child's glomerular filtration rate, an estimate was made of the excretion of endogenous creatinine. The blood level was 1·02 milligrammes per 100 millilitres, and 50 millilitres of urine, excreted in thirty minutes, contained creatinine to a value of 20 milligrammes per 100 millilitres. From these values a clearance of approximately 30 millilitres per minute is obtained.

Her weight on discharge from hospital was 34 pounds, and her height 37·5 inches.

Discussion.

It has been possible to follow this child's symptoms and progress from a very early stage. Symptoms began at about the time when she changed from a milk diet to one which included solids, though it is impossible to say whether the disease began then or merely became apparent, and the significance of the illness described as measles is obscure. In some respects there seem to have been progressive changes during the period of observation; for example, the systolic blood pressure at the first admission to hospital, when she was fourteen months old, was 80 millimetres of mercury, which may be considered normal for a child of that age, while in August, 1954, when she first manifested rickets, it was abnormally high (120 to

150 millimetres of mercury) and it has remained about 120 millimetres ever since. On the other hand her urine was at first free of albumin and microscopically normal, later all specimens examined contained albumin and casts, and later still these again disappeared.

The diarrhœa, which was the first and presenting symptom, is still present and unexplained. The response to the gluten-free diet was forgotten or overlooked when so many unexpected abnormalities were later discovered, and at some unrecorded stage, probably about December, 1954, when she began to do well in other respects, the diet was abandoned. However, reconsideration of her story suggests that the response should not be disregarded.

The only occasions when her stools have been normal in appearance during the period under review have accompanied the application of this diet in hospital. In the first month (April to May, 1953) of its use she gained four pounds in weight, and when it was reestablished in June of the same year she rapidly regained over a pound in a fortnight.

The exact role of wheat gluten in the ætiology of cœliac disease is not yet known, and even if its action can be linked with some defect in this child's intestinal absorption, her condition is certainly not cœliac disease. All that can be said is that she shows an impaired absorption of fat, though not of carbohydrate, that there is considerable water loss by the bowel, and that probably her hypophosphatæmia and hypokalæmia may be at least partly due to impaired absorption or increased loss by the bowel.

The abnormal results to glucose tolerance tests and the response to insulin have been constant. Can the child be properly regarded as a diabetic? What is the mechanism that prevents glycosuria?

The glycosuria occurring in Lignac-Fanconi disease and other syndromes of the Fanconi type is "renal"—that is, it is usually associated with normal blood sugar levels. Its mechanism is not clearly understood, but it is assumed to be due to a defect of renal tubular absorption. One child considered to be suffering from mild diabetes with a low renal threshold, who also was dwarfed, mentally backward and had rickets associated with hypophosphatæmia, has been described by Aiden and Nobel (1942).

Some other authors have reported high and prolonged blood sugar curves, and these reports have been tabulated by Bickel with the suggestion that this abnormal response may have been due to starvation (Bickel *et alii*, 1952). The child now under discussion was not starving, and she did not at any time show the sudden collapse during the making of glucose tolerance tests which Bickel considered to be due to a sudden fall in plasma potassium content on account of the administration of glucose.

It would seem that the absence of glycosuria despite very high blood sugar levels must be due either to a diminished glomerular filtration rate or to an increased tubular reabsorption.

The high blood urea levels found in the early stages might suggest impaired glomerular function, though further estimations made after treatment was instituted showed a fall to normal values. In order to obtain an indication of the glomerular filtration rate, an estimation of the excretion of endogenous creatinine was made. This indicated a glomerular filtration rate of about 30 millilitres per minute, which is probably about half the expected rate for a child of this age (Rubin *et alii*, 1949), and apparently this slow rate allows complete reabsorption of glucose to take place in the tubules. Even so, it is remarkable that sugar-free urine can accompany such high blood sugar levels. The hyperglycæmia is sensitive to quite small doses of insulin, smaller than one would expect in a case of diabetic hyperglycæmia of equal magnitude, and there have never been any symptoms or evidence of ketosis. It would therefore seem possible that the child is not a true diabetic and that the hyperglycæmia demands some other explanation. For the present, however, such an explanation and the possible linkage with the other symptoms remain matters for speculation.

Not only from the absence of cystine storage, but from numerous other observations, it is obvious that her condition differs completely from the Lignac-Fanconi disease described by Bickel and his co-workers. Yet in many respects, for example the mode of onset, the great thirst, the hypophosphatæmia, rickets, amino-aciduria and acidosis, there is sufficient resemblance to diseases of the "Fanconi" type to suggest that renal tubular defects may be playing some part in this child's complex disorder.

Only one measurement of the urinary phosphorus content was made and it was found to be within normal limits. The prevailing opinion seems to be that increased urinary loss of calcium and phosphorus does not occur except under treatment with massive doses of vitamin *D*, and that negative balances are due to faulty absorption from the intestine. While rickets is healed by massive dosage of vitamin *D*, normal levels of serum phosphorus are not achieved until the skeleton is replete with minerals, and reversion to low values occurs when massive therapy is ended and absorption from the intestine once more becomes deficient (Bickel *et alii*, 1952).

The most recent examination for aminoaciduria gave negative results both quantitatively and by chromatography. However, it is certain that a considerable amino-acid loss was occurring at an earlier stage, and in this respect at least a renal tubular defect could be postulated. The experience of Bickel and his colleagues was that prolonged alkalinization with sodium citrate led to cessation of aminoaciduria in all patients so treated (Bickel *et alii*, 1952).

The persistence of a very low serum potassium level, despite a high potassium intake, requires explanation. The first two measurements of urinary sodium and potassium contents in twenty-four-hour specimens indicated a relatively high potassium loss with sodium reabsorption, so that again a tubular defect in the absorption of potassium might be suspected. Even so, the renal losses of potassium hardly account for the low level in the serum in the presence of a high intake, so that failure of absorption or loss by the bowel would seem also to be responsible.

A more recent test showed sodium excretion in greater quantity than potassium. This test was made while she was losing the slight œdema she had on admission to hospital in March, 1956, and it is possible that fluctuations in the œdema may be associated with variations in the sodium and potassium content of the urine. There was certainly no œdema when the earlier measurements were made. But whatever the explanation for this much lower urinary potassium content at a time when the serum potassium content, though low, was virtually the same as at the time of the earlier tests, it would seem to indicate that efficient reabsorption of potassium by the renal tubules can occur, and therefore no permanent defect is present.

The persistently low serum potassium level may be due entirely to losses by the bowel, but it is of interest that, save possibly for her abdominal distension, the child shows none of the signs of muscle weakness *et cetera* usually associated with potassium depletion.

The apparent weakness, pain in the legs, and difficulty in walking were at first thought to be a result of hypokalæmia, which it will be recalled was first discovered at about the same time as the first radiological evidence of rickets. However, these symptoms rapidly disappeared with treatment and have not recurred, whereas the serum potassium level has remained low. It seems probable, therefore, that they accompanied the development of the rickets which must have begun when she started to grow. That was in April, 1954, just about the time of the last normal X-ray report. Why the child should have begun to grow when she did remains one of the many obscure features of this case.

The sustained improvement in the child's general condition since the institution of vitamin *D* and citrate therapy has been remarkable. She has shown a steady gain in weight and height so that today, although small, she is within the normal range for her age. Her mentality is normal and superficially she appears a healthy, lively and happy child. But evidence of continuing abnormality is

shown in the slight fluctuating œdema, and in the persisting abdominal distension, which though not gross is nevertheless apparent when she is undressed and for which she compensates by a characteristic lordotic posture and gait.

It must be admitted that despite the length of time for which this patient has been under observation her investigation is far from complete. There are various reasons for this; some investigations have been beyond the resources of the available laboratory facilities, while unusual or unfamiliar procedures have often had to be fitted into the programme of a laboratory already strained by the routine work of a busy hospital, and in addition the writer has been reluctant to subject the child and her parents to the strain of admissions to hospital and of laboratory tests more often than was absolutely necessary.

The real origin of all the abnormalities remains obscure, and while it is tempting to speculate on the possibility that they are all links in a chain of interdependent phenomena, the order in which the links should be placed and the possible existence of other vital but clinically invisible links remain a challenging puzzle awaiting solution.

Summary.

A case is described of a young child who presented with an unexplained diarrhœa and in whom growth was arrested for more than a year.

Investigation showed hypophosphatæmia (with rickets developing later), aminoaciduria, acidosis and a raised blood urea content, all of which decreased or disappeared during treatment with large doses of vitamin *D* and sodium and potassium citrates.

Hyperglycæmia, sensitive to insulin but unaccompanied by glycosuria, was also discovered. The absence of glycosuria appeared to be due to a low glomerular filtration rate.

A puzzling feature has been a persistently low serum potassium level.

There has also been evidence of disturbed adrenal function and of abnormality of the plasma proteins, and a suggestion that the diarrhœa might be relieved by the removal of wheat gluten from the diet.

The relationship between these phenomena remains obscure.

Acknowledgements.

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References.

AIDEN, R., and NOBEL, E. (1942), "Nephrotic Dwarfism and Rickets of the Low Phosphorus Type", *Brit. J. Child. Dis.*, 39 : 65.

ANDERSON, C. M., FRASER, A. C., FRENCH, J. M., GERRARD, J. W., SAMMONS, H. C., and SMELLIE, J. M. (1952), "Cœliac Disease: Gastro-intestinal Studies and the Effect of Dietary Wheat Flour", *Lancet*, 1 : 836.

BICKEL, H., BARR, H. S., ASTLEY, R., DOUGLAS, A. A., FINCH, E., HARRIS, H., HARVEY, C. C., HICKMANS, E. M., PHILPOTT, M. G., SMALLWOOD, W. C., SMELLIE, J. M., and TEALL, C. G. (1952), "Cystine Storage Disease with Amino-aciduria and Dwarfism (Lignac-Fanconi Disease)", *Acta pædiat.*, 42, Suppl. 90.

BICKEL, H., and SMELLIE, J. M. (1952), "Cystine Storage Disease with Amino-aciduria", *Lancet*, 1 : 1093.

BOYD, J. D., and STEARNS, G. (1942), "Concomitance of Chronic Acidosis with Late Rickets", *Am. J. Dis. Childhood*, 64 : 594.

DENT, C. E. (1952), "Rickets and Osteomalacia from Renal Tubule Defects", *J. Bone & Joint Surg.*, 34 (B) : 266.

FANCONI, G. (1954), "Tubular Insufficiency and Renal Dwarfism", *Arch. Dis. Childhood*, 29 : 1.

JACKSON, W. P. U., and LINDER, G. C. (1953), "Innate Functional Defects of the Renal Tubules, with Particular Reference to the Fanconi Syndrome", *Quart. J. Med.*, N.S. 22 : 133.

MCCUNE, D. J., MASON, M. D., and CLARKE, H. T. (1943), "Intractable Hypophosphatemic Rickets with Renal Glycosuria and Acidosis (The Fanconi Syndrome)", *Am. J. Dis. Childhood*, 65 : 81.

RUBIN, M. I., BRUCK, E., and RAPOPORT, M. (1949), "Maturation of Renal Function in Childhood", *J. Clin. Investigation*, 28 : 1144.

Appendix.

Blood Chemistry.

The following is a list of the blood chemical findings:

Serum Sodium Content.

16. 7.54.	340	mg	per 100 ml	= 148	mEq/L
26. 8.54.	325	„	„	= 141	„
22.10.54.	305	„	„	= 132	„
29.11.54.	315	„	„	= 137	„
26. 5.55.	320	„	„	= 139	„
14. 7.55.	310	„	„	= 134·7	„
1.12.55.	330	„	„	= 143·5	„
6. 3.56.	315	„	„	= 137	„

Serum Potassium Content.

16. 7.54.	9·5	mg	per 100 ml	= 2·4	mEq/L
26. 8.54.	11·5	„	„	= 3·0	„
22.10.54.	11·5	„	„	= 3·0	„
29.11.54.	13·5	„	„	= 3·4	„
7. 2.55.	13·0	„	„	= 3·3	„
26. 5.55.	11·0	„	„	= 2·8	„
14. 7.55.	9·5	„	„	= 2·4	„
1.12.55.	15·0	„	„	= 3·8	„
6. 3.56.	12.0	„	„	= 3·06	„

Serum Carbon Dioxide Content.

6. 9.54.	46%
20. 9.54.	44%
11.10.54.	41%
22.10.54.	40%
29.11.54.	54%
7. 7.55.	61%
14. 7.55.	72%
21. 7.55.	75%
1.12.55.	56%
6. 3.56.	52%

Serum Phosphorus Content.

4. 1.54.	2·4	mg per 100 ml.
26. 8.54.	3.2	„
16. 9.54.	5·0	„
20. 9.54.	5·5	„
22.10.54.	5·0	„
5.11.54.	5·2	„
29.11.54.	4·5	„
7. 2.55.	4·6	„
26. 5.55.	3·6	„
14. 7.55.	3·3	„
1.12.55.	5·3	„
6. 3.56.	4·2	„

Serum Calcium Content.

14.12.53.	9·5	mg per 100 ml.
26. 8.54.	9·0	„
16. 9.54.	10·3	„
20. 9.54.	10·5	„
22.10.54.	10·5	„
5.11.54.	10·6	„
29.11.54.	11·6	„
7. 2.55.	12·0	„
26. 5.55.	11·6	„
14. 7.55.	14·0	„
1.12.55.	11·5	„
6. 3.56.	13·0	„

Serum Alkaline Phosphatase Content.

12. 1.54.	26·0	King-Armstrong units.
3.12.54.	14·4	„

Serum Protein Content.

4. 3.53.	7·1	G/100 ml.
13.10.53.	7·9	„
11. 3.54.	8·0	„
16. 7.54.	8·3	„
7. 2.55.	7·8	„

Blood Urea Content.

16.12.53.	111 mg per 100 ml.
5. 1.54.	60 "
12. 1.54.	77 "
9. 2.54.	69 "
16. 7.54.	66 "
5.11.54.	57 "
7. 2.55.	54 "
26. 5.55.	42 "
14. 7.55.	30 "
1.12.55.	48 "

Blood Sugar (mg per 100 ml).

	Fasting.	½ hour.	1 hour.	2 hours.
13.11.53 (no insulin)	0·109	0·336	0·306	0·231
3.12.53 (insulin)	0·127	0·191	0·221	0·186
12. 1.54 (insulin)	0·129	0·166	0·166	0·152
28. 1.54 (no insulin)	0·105	0·241	0·241	0·196
11.10.54 (insulin)	0·100	0·232	0·255	0·186
9.11.54 (no insulin)	0·172	0·447	0·445	0·369
15.11.54 (no insulin)	0·114	0·286	0·374	0·328
29.11.54 (insulin)	0·122	0·206	0·261	0·241
8. 7.55 (no insulin)	0·141	0·191	0·307	0·216
26. 7.55 (insulin)	0·093	0·120	0·140	0·116

MULTIPLE CONGENITAL ANOMALIES ASSOCIATED WITH HYPERTROPHY OF THE PREPUCE OF THE CLITORIS AND THE FRENULUM.[1]

By Robert Vines,
Sydney.

The surgical habits of many races make it apparent that for sheer redundancy no portion of the male anatomy can equal the prepuce. How trivial then must we consider its inferior female homologue? So having had the grace to admit the redundancy and triviality of the subject, I hope you will allow me a few observations on three patients, examined recently by Professor Lorimer Dods and myself, in whom hypertrophy of the prepuce of the clitoris and frenulum was the major common abnormality in association with a variety of other congenital malformations.

Case I.

H., the youngest of a family of four children, was born after a normal pregnancy and labour; she weighed eight pounds one ounce at birth. Her parents and siblings were healthy. Her progress up to the time when she was first examined at the age of fifteen months was satisfactory. At that time she could walk, weighed 20 pounds, was thirty and a half inches in height and had normal trunk-limb proportions. Her nasal bridge was wide and depressed and the ears, set low on the head, were small, the superior portion of the left ear having a "crumpled" appearance. There was unusual prominence of the heels posteriorly and syndactyly of the third, fourth and fifth toes was present bilaterally. The prepuce of the clitoris and frenulum, which was said gradually to have decreased in size, was an organ nearly three-quarters of an inch in length, half an inch in width and one-third of an inch in thickness. In other respects the vulval anatomy appeared normal for her age, nor were any other physical abnormalities noted. At that time her osseous age was normal, her twenty-four-hour 17-ketosteroid excretion was 0·7 milligramme, and a vaginogram indicated the presence of a vagina having normal dimensions and relationship to the bladder.

When examined again at the age of twenty-two months she was said to have been well, but weighed only 22 pounds and had a clumsy gait. She was unable to run. It was said that her micturition always had a dribbling character. Her osseous age was again normal, as was an excretion pyelogram and a micturition cystogram. The blood urea content was 32 milligrammes per 100 millilitres. Cystoscopy revealed no abnormality, and at the end of the one and a half inches long vagina was an apparently normal cervix. The leucocyte chromatin pattern was "female".

Case II.

C. was admitted to the Royal Alexandra Hospital for Children under the care of Dr. D. G. Vickery when three days old. Her parents and siblings were healthy. She was born by low forceps delivery after a normal pregnancy and weighed five pounds. Oxygen was administered because of her poor condition at birth and on the third day of life after a series of convulsive movements of the face and limbs her temperature was noted to be 102·5° F.

Examined at this time, she was found to be pale and ill. Her facies was unusual in that the mandible was small, the nasal bridge was flat and wide and the ears were low set and large. Just behind the vertex was an area of very thin hairless skin, one and a half inches by half an inch, which on palpation gave the sensation of there being a gap in the tissues deep to it. Extension at the elbows was limited to 150°. There was mild right *talipes calcaneo-valgus* and left *talipes equino-varus*. Syndactyly of the third, fourth and fifth toes was present bilaterally. The prepuce of the clitoris and frenulum (Figure I) was

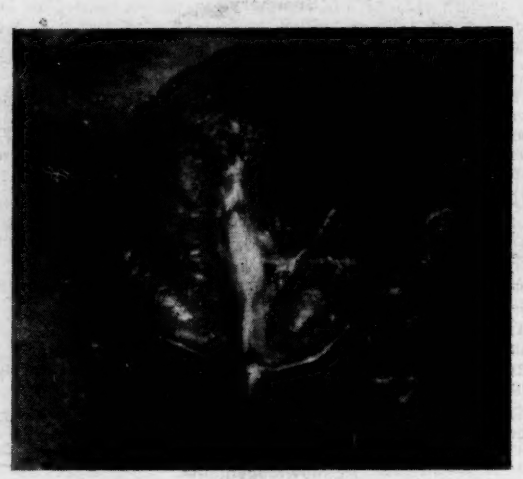

Figure I.

External genitalia in Case II, showing the four terminal digitations of the hypertrophied clitoral prepuce.

identical in size and shape with that in Case I. The rest of the vulval anatomy appeared normal.

X-ray photographs of skull, elbows and pelvis revealed no abnormality, but in the chest radiograph the position of the ribs was noted to be unusual, suggesting incomplete expansion of the lungs.

She sucked quite well, but failed to thrive and when eight weeks old developed pneumonia. At this time a soft systolic murmur was audible. The fever was not controlled and she died at the age of eleven weeks. Blood counts were normal on several occasions and her leucocyte chromatin pattern was "female". Unfortunately a post-mortem examination was not performed.

Case III.

P. (Figure II), a patient of Mr. E. S. Stuckey, was the youngest of three children. Her parents and siblings were well. Her birth weight was seven pounds, and though her progress was said to have been satisfactory, when examined at the age of twelve months she weighed only 18 pounds. Her height was 30 inches and trunk-limb proportions were normal. She had sat up at the age of eight months but was not yet crawling; she still had a palmar type of grasp, indulged in much body rocking and appeared mentally dull. A wide flat nasal bridge,

[1] Read at the annual meeting of the Australian Pædiatric Association, Canberra, April 13 to 16, 1956.

prominent eyes and low set "bat" ears gave her an unusual appearance. Her skull was brachycephalic and her large anterior fontanelle had two anterior cornual prolongations. Bony fixation of the elbow joints in .. 110° position was present and this was shown radiologically to be due to failure of formation of the radio-humeral joints. Deficient extension at the metacarpo-phalangeal joints was associated with a tendency for the hands to be held in ulnar deviation. Bilateral *talipes equino-varus* and flat feet of the so-called "vertical talus" type were present. The osseous age was within normal limits. The blood hæmoglobin content was 9·1 grammes per 100 millilitres and red cells numbered 5,100,000 per cubic millimetre. Her twenty-four-hour urinary 17-ketosteroid excretion was 0·5 milligramme and her leucocyte chromatin pattern was "female".

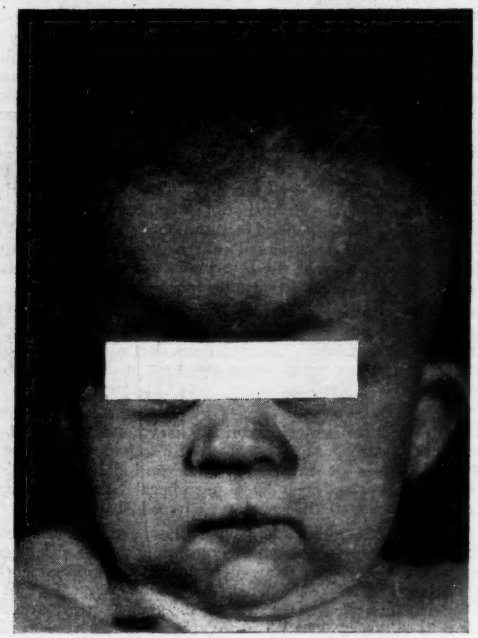

FIGURE II.

The face in Case III, showing the wide depressed nasal bridge and low set ears common to all three cases.

Examination of the patient under anæsthesia revealed a prepuce of the clitoris and frenulum one inch long, three-quarters of an inch wide and half an inch thick (Figure III), but the anatomy of the genitalia was otherwise normal. During this examination she suffered cardiac arrest and was resuscitated by cardiac massage only to die three days later without recovering consciousness. At a coroner's post-mortem examination no further abnormalities were noted apart from the presence of a small diverticulum of the bladder on the right side just above the junction of the bladder with the ureter. Dr. Douglas Reye examined the ovaries, uterine tubes, uterus and adrenals and considered them normal both macroscopically and histologically.

The Genital Abnormality.

The organ termed an hypertrophied prepuce of the clitoris and frenulum (Figure I) was identical in form and nearly identical in size in these three patients. Dorsally this structure was convex longitudinally and transversely, while ventrally it was deeply grooved longitudinally so that it might be described as folded like a leaf on its stem. Distally it terminated in four digitations, which together with a ventrally situated ridge of tissue enclosed a small pit. The whole organ was so soft and flaccid as in no way to suggest the firm consistency of a normal or hypertrophied clitoris. Indeed the *glans clitoridis* could not be identified with any certainty either visually or by palpation.

The difference in morphology between this structure and a normal or hypertrophied clitoris appeared at first so great as to make its embryogeny inexplicable, but further observations appeared to offer a reasonable explanation. An infant was examined who in the first three weeks of life had as her sole physical abnormality an organ

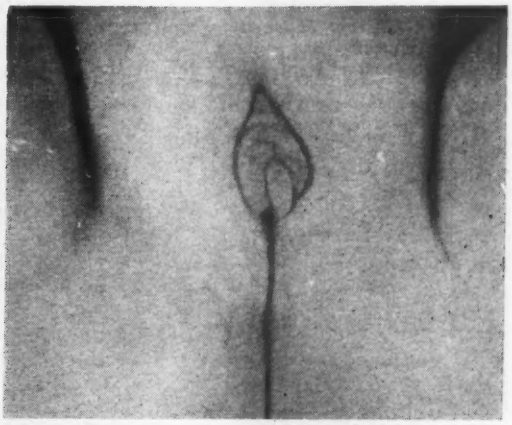

FIGURE III.

Hypertrophied prepuce of clitoris and frenulum in Case III, giving a better impression of the looseness and flaccidity of the organ.

exactly similar in size and form to those in the three patients described above, but at nine months of age her genitalia were normal. This made it evident that an hypertrophy of normal structures could explain the occurrence of the malformation and that its origin did not necessarily have to depend on some basic deviation from normal genital embryogeny. It was noted, too, that the prepuce of infant girls with congenital adrenal hyperplasia ended in a broad central notch between marked lateral convexities. Popper showed that in hypospadiac males preputial development follows the female pattern and the prepuce in this condition shows a central notch bounded by lateral convexities which may fairly readily be considered analogous to the two medial digitations of the abnormal structure described earlier. To find an explanation for the origin of the paired lateral digitations it is necessary to observe the anatomy of the anterior extremities of the *labia minora* with more precision than appears to have been done by many generations of anatomists, for they have left unnamed a tubercle sometimes present at the anterior end of each *labium minus* from whose supero-medial aspect arises the frenulum. Certainly the great normal variation in these structures and the frequency of adhesions in this region do not permit identification of these prominences in all children, and it is only when hypertrophy is present, as is often the case in the newborn (Figure IV), that the analogy with the lateral digitations of the organ described above is obvious.

Discussion.

The three children described have in common the same genital deformity and a variety of malformations, the most prominent of which are skeletal. In a search of available literature no reports of a comparable group of cases were found. The two infants described under the

title of leprechaunism by Donohue and Uchida differed in their lower birth weight, hirsuties, mammary enlargement, absence of skeletal abnormalities and less definite clitoral abnormality, and in the presence of changes in the ovaries, liver and kidneys. The two children described by Evans as being further examples of leprechaunism differed in showing mammary enlargement, absence of clitoral abnormality in one, retarded osseous age, and the absence of any skeletal deformity in one.

If syndactyly only is considered, a developmental disturbance occurring between the sixth and eighth weeks of pregnancy may be postulated. However, at this period neither the clitoral prepuce nor the radio-humeral joints have developed, and some noxious influence continuing to exert an effect at least till well on in the second trimester of pregnancy must be invoked to explain the occurrence of malformations in these regions. There was no evidence in the family histories to enable this noxious influence

FIGURE IV.

External genitalia of normal female infant one month old. A and B indicate the tubercles which in the cases described are represented by the medial and lateral digitations of the hypertrophied clitoral prepuce.

to be ascribed to the presence of abnormal genes. While development in the presence of excessive œstrogens might account for the occurrence of hypertrophy of the pupice of the clitoris and frenulum, it does not provide an explanation for the occurrence of the other abnormalities.

Summary.

Three infants are described in whom pronounced hypertrophy of the prepuce of the clitoris and frenulum was present.

There was a variety of associated malformations, mainly skeletal deformities together with some facial resemblance and a varying degree of failure to thrive.

It is suggested that the noxious influence responsible for producing this syndrome exerts its effect for a period extending from at least the second to the fifth month of fœtal life.

References.

DONOHUE, W. L., and UCHIDA, I. (1954), "Leprechaunism: A Euphuism for a Rare Familial Disorder", *J. Pediat.*, 45: 505.

EVANS, R. R. (1955), "Leprechaunism", *Arch. Dis. Childhood*, 30: 479.

POPPER, R. (1937), *"Die Entwicklung des Praeputium Clitoridis mit Bemerkungen über die Homologisierung von Praeputium Penis und Praeputium Clitoridis und über das Praeputium der Hypospaden"*, *Zeits. f. Anat. u. Entwicklungageschicte*, 107: 378.

Reviews.

Pædiatrics for the Practitioner, edited by Wilfrid Gaisford, M.D., M.Sc., F.R.C.P., and Reginald Lightwood, M.D., F.R.C.P., D.P.H.; 1954. London: Butterworth and Company (Publishers), Limited. Sydney: Butterworth and Company (Australia), Limited. Volume II. 10" × 7", pp. 574, with 83 illustrations. Volume III. 10" × 7", pp. 682, with 159 illustrations. Price: £17 10s. for set of four volumes.

THESE two volumes, together with a separate index, complete what is intended by the publishers to be a comprehensive work covering the whole field of pædiatrics, at what might be described as the general practitioner level. To this end there is a fairly detailed description of disease and abnormalities as they occur in childhood, including many common and minor conditions so often not mentioned in standard text-books. This aspect of the publication could have been made even more valuable to the practitioner if sections discussing the differential diagnosis of the commoner symptom complexes seen in children had been included.

Treatment is discussed in any detail only in so far as it can be given in the home or consulting room. If the condition is one for which hospitalization is likely to be needed, then usually the bare outline of treatment only is given. It is this aspect of the work, previously mentioned in the review of Volume I, which is likely to be most disappointing to the general practitioner in this country, who is accustomed to assuming a greater responsibility for the care of his own patients, however ill, than apparently is his British counterpart. The frequent repetition of the statement that the child should be sent to hospital without further details of management being given is very unsatisfying. For the same reason discussion of the investigational approach to different problems, and the interpretation and assessment of the results obtained, are rather limited.

Volume II contains sections on endocrine disorders, including a chapter on obesity; diseases of the alimentary tract; the liver and biliary system; steatorrhœa and allied conditions; the upper and lower respiratory systems, including the ear; tuberculosis; the genito-urinary system; psychological and mental disorders.

Volume III contains sections on the nervous system; allergic diseases; skin disorders; the eyes; infections and infectious diseases; diseases of muscles; bone and joint conditions; unclassified diseases, including peripheral vascular disease, pink disease, collagen diseases and sarcoidosis.

Despite the deficiencies mentioned above, and in the review of Volume I, a real and on the whole fairly successful attempt has been made in these three volumes to provide a work of reference covering the whole field of pædiatrics. Most of the medical, psychological and social problems are mentioned, including the influence of hereditary factors, that one is likely to meet in the care of children. Often the information is scanty, and much less than one would wish for, but it will be rare not to be able to find some mention of most subjects in this field.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Thiopentone and Other Thiobarbiturates", by John W. Dundee, M.D., F.F.A.R.C.S., D.A.; 1956. Edinburgh and London: E. and S. Livingstone, Limited. 8½" × 5½", pp. 319, with illustrations. Price: £1 2s. 6d.

Intended for all "physicians who are interested in intravenous anæsthesia".

"Sir William Arbuthnot Lane, Bt., C.B., M.S.: An Enquiry into the Mind and Influence of a Surgeon", by T. B. Layton, D.S.O., M.S.; 1956. Edinburgh and London: E. and S. Livingstone, Limited. 9" × 6¼", pp. 136, with nine illustrations. Price: 21s.

The life of a man who, the author claims, was unique.

"Trace Elements in Human and Animal Nutrition", by E. J. Underwood; 1956. New York: Academic Press, Incorporated. 9" × 6", pp. 439, with illustrations. Price: $9.50.

Written for those who plan to specialize in nutrition or who are already specialists in nutrition.

The Medical Journal of Australia

SATURDAY, AUGUST 18, 1956.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

CHILDHOOD AND MENTAL HEALTH.

PÆDIATRICS may be looked at from two points of view. In the first place it represents a highly specialized field of study whose practitioners need exceptional qualities of heart and mind if they are to be successful in the true sense of the term. Secondly, pædiatrics stands in fundamental relationship to every other aspect of medicine—"the child is father to the man" in disease as well as in health. This has been discussed in these columns on a previous occasion. This issue of the journal is given over to an account of the annual meeting of the Australian Pædiatric Association held at Canberra earlier this year. At this meeting seventeen subjects were discussed. Six of the contributions are published in full and the others are set out more or less in abstract form with the discussions. Attention is drawn to the wide range of subjects that were covered, and, of course, it is clear that the number of subjects that might be chosen for such a meeting is legion. In the present instance it so happens that no special psychological subject was selected. It is therefore fitting that reference should be made to mental health in childhood.

The opportunity to do this arises with the publication by the Australian Pre-School Association of a report of its seventh biennial conference held at the University of Melbourne from August 27 to September 2, 1955. The subject of the conference was "Childhood and Mental Health". The fact that this report comes from the Pre-School Association recalled at once a publication of 1946 by John Bostock and Edna Hill entitled "The Pre-School Child and Society: A Study of Australian Conditions and Their Repercussions on National Welfare". This was discussed at some length in these columns on December 14, 1946. Those who have access to Bostock and Hill's work might well consider it in conjunction with the present report. Though the present report deals with the whole subject of childhood and mental health and not only with the pre-school aspect, some of the main points made by Bostock and Hill may be recalled. They insisted that the child's development should be planned, so that it should not be side-tracked by the multiple sensations and impressions which are part of everyday life. Discussion of this led to mention of the need for the education of parents, without which planning for the child would be inadequate. From this reference was made to housing and nutrition, to the need for adequate child endowment and to the national use of kindergartens.

His Excellency the Governor-General, Sir William Slim, opened the Pre-School Association's Conference, and as we have learned to expect from him, made some wise and appropriate remarks. He deplored the fact that at the present time more and more prominence was given to material things, and added that much of our education, especially higher education, was devoted to teaching young people how to make a living rather than how to live. He said that the greatest need for improvement was not in materials or method, but in humanity itself. That was why the first contacts of the child with society were so vitally important. Dr. Guy Springthorpe, who presided at the conference, discussed the meaning of the term "mental health". He said that, at the risk of being taken to task, he would describe mind as "that part of everyone which feels and thinks and regulates behaviour; where feeling equates with emotion, thinking with intellect and behaviour is what we do and, in a sense, what we are". He laid stress on the importance of feeling, or the emotional part of the mind, and its influence on behaviour. The proper balance of the emotions is in his opinion the most important factor in healthy mental development. Most vital are the emotional interrelations in the first few years of life, the key persons in order of importance being the mother, the father and other members of the family. From this it is clear that the importance of the family cannot be over-estimated. Dr. Springthorpe, quoting from an article by Professor E. Saint, insisted that the need was not the gaining of more detailed knowledge of child phantasy life, but the application of knowledge already gained to the education of parents, school teachers and doctors. Professor R. D. MacCalman, Nuffield Professor of Psychiatry at the University of Leeds, England, who visited Australia at the invitation of the Australian Pre-School Association, addressed the conference; he also gave a talk as "Guest of Honour" over the national broadcasting network; this address is included in the report. Professor MacCalman said that the hope of the future lay in the early years of life. The child required firmness to protect him against the tyranny of his own egocentric emotions and drives. The child quickly sensed whether his parents were affectionate, warm, trustworthy, cooperative and firm, or whether they were troubled, doubt-ridden, resentful, hateful and potentially dangerous to himself. In this

respect young children were often wiser than grown-ups. The aim in general (Professor MacCalman quoted John Bowlby) had to be the protection and development, at all levels of human society, of serene, affectionate and satisfying human relationships, and the reduction of hostile tensions in persons and groups. Professor MacCalman thought that the spiritual development of the child should be considered in relation to mental health, and we must agree that to omit such aspects of the child's being would be a serious handicap to him. Professor MacCalman states that he believes sincerely that a religious faith which permeates the mind and feelings of a parent contributes in a unique way to his ability to transmit a sense of trust to his child. It is interesting that Professor MacCalman quotes words of Sir Charles Morris: "The educational system should turn from the comparatively easy task of producing scientists and technologists to the much more difficult task of educating young people to be good parents."

There are many facets of this subject dealt with in the present report, and almost every one of them would provide groundwork for a discussion. Reference will be made to only one more contribution—that of Christine Heinig, who is on the staff of the American Association of University Women, Washington, D.C. She discusses educational trends in the United States of America. The inclusion of a paper on education will remind us all that the securing of mental health in childhood is not a single act, but the beginning of a long-continuing process, for who can say when we have learned and assimilated all that we need to know of health? Be that as it may, it will be useful to reproduce what Heinig calls the five "priorities" for learning. They have been approved by the American Association of University Women. The first is that children shall learn to be confident, to feel adequate to the job ahead. Secondly, children have to understand their world and to learn ways of controlling it. Thirdly, they are to trust people and to be friendly in their relations with them. Fourthly, the children are wanted to develop a feeling of responsibility for participating politically in democratic government. Lastly, it is desired that children shall understand and have faith in the principles underlying the democratic way of life. Most people will accept the first three of these priorities, but many, even though they may be dyed in the wool democrats, will question the wisdom of the introduction of political considerations into the discussion of mental health in general.

Even though reference to this report has been incomplete, enough has been stated to allow readers to form some idea of what it is all about. The fact to be emphasized is that pædiatrics which neglects psychological considerations is incomplete. We have seen that mental health in childhood is to be actively sought, but that in the seeking much attention has to be paid to parents in their personal and family relationships. It might be argued that in these circumstances pædiatrics goes beyond its recognized confines. While this might be true up to a certain point, it has to be remembered that if parents have had adequate pædiatric psychological treatment as children, they will not have to be taught how to deal with their own growing children. Expanding Sir William Slim's statement a little, we may say that children need not only healthy bodies that they may earn a living, but also healthy minds so that they may learn how to live. It is the duty of pædiatric specialists to see that this is done. It is to be hoped that papers on the care and cultivation of children's minds were not deliberately excluded from the last programme of the Australian Pædiatric Association's meeting. At the meeting before the last, one or two papers on the psychological aspect were presented. To avoid any suggestion of short-sightedness in this matter, those who plan the Association's meetings would do well to include at each annual meeting at least one discussion on some aspect of the mental health of children.

Current Comment.

HIATUS HERNIA IN CHILDREN.

The clinical significance of hiatus hernia in childhood is stirring more interest as improved diagnostic methods reveal its growing incidence amongst children who are being investigated for vomiting, dysphagia, hæmatemesis and related dyspeptic symptoms. During recent years, as more cases were studied in childhood, it was realized that although the symptomatology in infants differed from that in adults, the basic nature of pathological events was similar in both groups. There was little conception of the natural course of the condition in childhood until Smellie, Carré and Astley in 1954 published their results of a series of 112 cases of minor intrathoracic stomach in childhood. They emphasized the benign course in the majority of cases, stating that less than one in ten of these children developed œsophageal complications in later childhood.

In this issue there appears a study on gastro-œsophageal reflux in infancy and childhood by Frieda E. Plarre, who writes from the Royal Children's Hospital, Melbourne. At the same time we wish to remind readers of the three papers published in the issue of July 28, 1956, by W. E. King, A. E. Piper and K. N. Morris on hiatus hernia, which were read at a meeting of the Victorian Branch of the British Medical Association. These papers did not deal expressly with infancy and childhood, but they should nevertheless be read in conjunction with Plarre's paper. Plarre's four conclusions should be noted: (i) A hiatal defect may be present early in life without necessarily causing reflux. (ii) If control is started early enough and the symptoms of reflux and of gastro-œsophagitis have subsided, the condition of simple cardio-œsophageal relaxation or of minor intrathoracic stomach may return to normal. (iii) Reflux may persist long after symptoms have subsided under medical control and also after adequate surgical repair has been effected. (iv) The diagnosis of actual or impending fibrous stricture and its differentiation from narrowing of the œsophagus due to spasm or œdema are difficult in a young child.

In addition to the contributions from Melbourne attention must be directed to the result of a five-year study of hiatal hernia in 58 children which has just been published by Gregers Thomsen,[1] of Copenhagen. His work is primarily a radiological study, but he also makes available full clinical data demonstrating aspects of the natural history, and observations on the comparative value of surgical and conservative measures in managing these children. He classifies the patients in a simple practical manner: first, a group of five patients with para-œsophageal hernia without reflux; secondly, a group of 27 with sliding hiatal hernia without œsophageal complications; and thirdly, a group of 26 with sliding hiatal hernia and œsophageal complications. The clinical pattern in the uncomplicated group was similar to that described by Carré and Astley, namely, complete recovery of some patients, while others had a more prolonged course with

[1] *Acta radiolog.*, 1955, Supplementum 129.

periodic exacerbations of symptoms before improvement was maintained. Fibrous stricture and shortening of the œsophagus were rarely seen as complications before the patients were one or two years of age. In more severe and complicated cases, eleven of the patients were followed with conservative management only, and Thomsen notes that after years of worrying symptoms and frequent admission to hospital, these patients often proved surprisingly little troubled by their symptoms in early adult life when they were liable to periodic recurrences of lessened severity. He refers briefly to the importance of psychic factors in these children.

Of those children with uncomplicated hiatal hernia who were managed conservatively some recovered quickly, while others required more exacting and prolonged treatment. Surgical treatment in the form of herniotomy was disappointing in the prevention of complications and did not shorten the expected period of recovery. In Thomsen's series of 58 patients, 24 were treated conservatively and 34 were subjected to surgery. Of the latter group eleven had a second operation, so that in all, 45 operations were performed on 34 children. Three had phrenic avulsion alone, three had œsophageal excision with œsophagogastrostomy, and the remainder had herniotomy. Of the 39 herniotomy operations, two were performed by the abdominal route, in 27 repair of the crura and phrenoœsophageal ligaments was carried out, and in ten cases repair of the crural sling was combined with fixation of the fundus by the thoracic approach. Thomsen concludes that herniotomy may be performed only after a thorough trial of conservative treatment, and then not before the end of the first or second year of life in cases in which signs and symptoms are present; he draws this conclusion on the assumption that persistent reflux may result in œsophageal complications later.

On following up three patients whose hiatal hernia was characterized by fibrous stricture and penetrating ulcer of the œsophagus, Thomsen finds the results of radical excision encouraging. His follow-up period has been fairly short, but he quotes other series in which the period was longer after the same operation and states that the results were satisfactory. He stresses the need for careful selection of cases for excision, for he holds that radical surgery will give the best results after fixed fibrous deformity of the œsophagus has resulted and the active inflammatory changes of œsophagitis have subsided. In young children a long period of observation of at least several months, and sometimes years, may be necessary to differentiate between recurring spasm or œdema on the one hand, and permanent fibrous scarring of the œsophagus on the other.

Some aspects of the pathology of hiatus hernia and œsophageal fibrosis still need further clarification. That reflux is not the only factor responsible for œsophagitis and its symptomatology is shown by those patients who have lost their symptoms after excision, yet have very free reflux into the upper part of the œsophagus without developing further œsophagitis. Also in those cases in which conservative management has been adopted, symptoms may have completely abated for months or years, while reflux and herniation are found to persist for long periods when radiological examination is carried out. No œsophagitis is present at this stage on clinical or endoscopic examination. The limitation of herniotomy techniques in controlling reflux may be partly explained by the fact that the crural sling, phreno-œsophageal ligaments and œsophago-gastric angle are not the only factors in normal physiological competence. The lack of direct relation between hernial deformity, reflux and œsophagitis indicates the necessity for a wider approach to the study of the pathology of œsophagitis. Both P. M. Peters and K. V. Lodge have reported useful post-mortem studies chiefly in adults, but the interpretation of mucosal changes is difficult in young children without more extensive serial biopsy studies, which are difficult to carry out.

The importance of psychic factors is hinted at by Thomsen, and by many writers in adult studies. It is especially important to enlist the confidence and cooperation of parents during the treatment of young children, particularly when the course of symptoms is likely to recur and perhaps to be prolonged.

Peptic ulcer sometimes complicates this syndrome in children as in adults. Thomsen describes one case of perforated ulcer in a para-œsophageal hernia in which a duodenal ulcer developed after treatment of the hernia and its ulcer; this suggests that other factors are present which predispose to ulcer besides the predilection of the mucosa in a hernia. The periodical nature of œsophagitis recalls a similar characteristic of symptoms from peptic ulceration elsewhere, the ætiology of which is still far from being completely understood.

Thomsen and Astley have both described in full the radiological features of hiatal hernia in childhood. Both have stressed the importance of fluoroscopic examination, of repeated preparation of films and examinations, of positioning, and of methods of eliciting reflux. The limitations of radiological diagnosis are imposed mainly by the limitations of clinical interpretation. As we achieve further enlightenment on the problems of the pathology and physiology of the gastro-œsophageal region, with its intricate nervous and neuro-vascular arrangement, further clarification of the clinical significance of hiatal hernia may be possible. In the meantime, if we declare that surgical operation is to be our refuge when medical treatment fails, we should see to it that the medical treatment is adequate.

A NEW TREATMENT FOR WARTS.

THE different kinds of treatment for warts are many. The basic differences in the types of treatment, including excision, cauterization, radiotherapy, hypnosis and confident hope, exemplify the strangely mingled conflict between potential virus infection, chronic irritation and the psychosoma. Warts are particularly troublesome if they appear on weight-bearing areas, and may cause considerable incapacity and recur with provoking regularity. M. D. Steinberg[1] suggests that many tragic sequelæ have followed the use of X-ray therapy or of radium for warts, which tend to be particularly radio-resistant. Steinberg has noted that diabetics rarely develop warts and that xanthochromic diabetic persons never do so. Accordingly, he carried out his investigations on the presumption that, in such patients, a faulty utilization of vitamin *A* resulted in higher vitamin *A* skin levels. A special solution of vitamin *A* was devised containing a small amount of fatty oil and α tocopherol. This solution contained 50,000 units of the vitamin per millilitre, and it was found possible to place it in ampoules and to autoclave it for sterilization. The use of a control solution of the ingredients, but without the vitamin, failed to have any effect in the treatment of the warts. The normal technique was to use a local anæsthetic and then, by means of a tuberculin syringe, to inject the vitamin solution slowly into the base of the verruca, with care to avoid leakage away from the injection site. The initial dose did not exceed 0·1 millilitre per square centimetre of the verruca's area. Injections were given weekly, and were sometimes increased to double the aforementioned dose. Steinberg found that involution of the wart began within a few days, and that after two to eight weeks of these injections the lesions regressed completely, leaving no evidence of alteration in the normal skin. Pain usually disappeared early and no limitation of activity was needed throughout the course of treatment. Among 300 patients so treated there were only seven failures, and these Steinberg ascribed to the physical characteristics of the wart itself. No other treatment was given, and despite the fact that some of the verrucous areas were very large, no recurrences have taken place. How far the effectiveness of the treatment can be ascribed to injection at the base of the wart is not clear, but the idea is interesting and seems to have a great advantage, as it appears to be safe.

[1] *Surgery*, April, 1956.

Abstracts from Medical Literature.

PÆDIATRICS.

State of the Lungs at Birth.

E. L. POTTER (*J.A.M.A.*, December 3, 1955) states that the first stage of lung development, occupying the first half of fœtal life, is one of increasing elongation and ramification of the original endodermal lung bud. Each terminal bud incites mesodermal proliferation, so that it becomes sheathed in connective tissue. With progressive multiplication of the buds, their external surfaces become more closely approximated, and the connective tissue sheaths lose their individuality. The second phase is one of vascularization. Capillaries penetrate the endodermal lining of the buds and lie in direct contact with the lumen. The author points out that during development the walls of the alvèoli are not closely apposed, and that a lumen is always present. The respiratory centre differentiates very early in embryonic life and immaturity of it is never a cause of the failure to commence respiration. It is thought that extra-uterine respiration is merely a direct continuation of intrauterine activity with ready provision for the entry of air down lumina already patent in the infant's pulmonary tree. "Resuscitation" does not entail setting off some trigger mechanism. Oxygen must be supplied until whatever has depressed respiration ceases to act, and it is best introduced in some way that closely simulates the infant's normal respiration. Direct depression of the respiratory centre by anoxia, depressant drugs or toxic conditions of the mother are the commonest causes of respiratory depression. Except in the case of malformations or in the presence of pneumonia, a local disturbance of the lungs is almost never responsible for post-natal apnœa.

Leprechaunism.

P. R. EVANS (*Arch. Dis. Childhood*, December, 1955) describes two children who he suggests belong to the group recently described as suffering from leprechaunism. Under this title, Donohue and Uchida (1954) described two sisters with a characteristic facies, hirsuties and large ears, and with hyperplasia of the mammary ducts, clitoris and ovaries, a failure of growth, and an increased hepatic glycogen and insulin content of the pancreas. One of Evans's patients was observed to the age of nine months. This infant resembled Donohue and Uchida's patients in her facies, her mammary and clitoral enlargement, and her defective growth, and in the presence of cystic changes in the ovaries. By contrast, the birth weight was normal, there was no hirsuties, and no changes in the liver and pancreas. The author's second case was that of a mentally retarded girl aged two years and nine months with large ears, mammary hyperplasia, increased liver glycogen, large cystic ovaries and decreased bone age. Her birth weight had been normal, her appearance was not typical, and her clitoris was not enlarged. The suggestion is made that genetic abnormalities may cause abnormalities of the face, ears and ovaries, and that the excessive œstrogen production by these abnormal ovaries may be directly responsible for the production of mammary and clitoral enlargement, and may also be responsible for slowing growth, increasing insulin production and inducing hypoglycæmic unresponsiveness through inhibition of the production of growth hormone by the pituitary gland.

Hypertonic Dehydration.

W. B. WEIL AND W. M. WALLACE (*Pediatrics*, February, 1956) state that of dehydrated infants, 10% are found to be hypotonic and 20% hypertonic, with regard to serum sodium concentration. The hypotonicity of bodily excretions, particularly in infantile gastro-enteritis, brings about the occurrence of hypertonic dehydration. Clinically these infants may show little to suggest the presence of dehydration; skin turgor and eyeball tension are usually normal. However, disturbance of the nervous system is common, and takes the form of lethargy or coma, hypertonicity of muscles and convulsions. Dehydration in these infants mainly affects the intracellular compartment. Transient renal dysfunction is present as, despite oliguria, the specific gravity of the urine remains low, and low urea clearances have been demonstrated. It is not understood why this renal dysfunction should occur. The rapid adjustment of serum sodium levels often leads to convulsions, so that gradual repair over a two to three days' period is recommended. Solutions containing 50 to 65 milliequivalents per litre of sodium and 35 to 45 milliequivalents per litre of chloride are suggested. As the authors found no significant deficiencies of potassium in balance studies, they avoid the addition of potassium to the solutions administered.

Prognosis of Tuberculosis in Childhood.

N. LEVIN (*Am. Rev. Tuberc.*, October, 1955) reports the result of a follow-up study of 434 children with verified or suspected intrathoracic tuberculosis. The follow-up period ranged from sixeen to twenty-four years. The children were up to fifteen years old. Special study of the 254 children who were initially found to have active tuberculosis revealed that 5% still had active disease and 13% had died of the tuberculosis. The mortality rate of those children who were originally found to have primary tuberculosis was 7%, while that of the children who were originally found to have post-primary lesions was 63%. In the "primary" group the mortality rate increased with the age of the child at diagnosis, but in those with post-primary lesions the trend was reversed, except in the case of the children who contracted tuberculosis during puberty. Death from meningitis was more common in the "primary" group; in both groups death tended to occur in early childhood. The results of this study reveal that a decline of almost 50% in the mortality rate of childhood tuberculosis has occurred in the Länssanatoriet Hospital, Uttran, Sweden, between the time of Lundquist's follow-up study of children admitted there between 1910 and 1920 and the present time.

ORTHOPÆDIC SURGERY.

Grafts for Digital Flexor Tendon Injuries.

G. PULVERTAFT (*J. Bone & Joint Surg.*, February, 1956) has reviewed a series of 149 consecutive cases in which the flexor tendon of the finger or thumb was grafted and has analysed the results. A description is given of the technique which has been evolved. The author found that replacement of a divided tendon of the *flexor digitorum profundus*, in the presence of an intact *flexor digitorum sublimis* tendon, restored a useful range of movement in 80% of cases. Replacement of both *flexor digitorum profundus* and *flexor digitorum sublimis* produced a good result in 70% to 80% of cases. Replacement of a divided *flexor pollicis longus* tendon gave good results in 85% of cases. The particular tendon used for the graft did not materially influence the result, but there are special indications for the use of the different tendons. The choice of either splintage or early movement after operation does not appear to have a significant bearing upon the result. The most important factor in determining the result is probably a precise and gentle surgical technique and complete hæmostasis. Minor differences in method are of little importance. The failures in this series were attributable more to faulty performance of the operation than to any other single factor.

Metallic Transfer in Orthopædic Surgery.

F. P. BOWDEN, J. B. P. WILLIAMSON AND P. G. LAING (*J. Bone & Joint Surg.*, November, 1955) have demonstrated by the use of radioisotope techniques that whenever an orthopædic appliance is inserted into the body tiny fragments of the instruments used to handle it become detached and welded on to the surface of the buried metal. There is evidence that these particles of non-passive tool-metal may cause a small but continuing dissolution of the stainless metal to which they are attached, and that this dissolution, although too small to be detected as visible corrosion, may produce an adverse tissue reaction. In samples of human tissue, taken from sites adjacent to buried metal, the greatest level of tissue reaction and the highest concentration of iron were found near those parts of the appliances that had been handled with the tools and had received the greatest amount of transferred metal. Spectroscopic analyses of similar samples confirmed that the concentration of metal in the tissues surrounding a buried appliance correlates closely with the distribution on its surface of transferred tool metal. Particularly high concentrations of chromium, nickel and cobalt were found near regions where the transfer had been heavy. The dissolution was not limited to the non-passive foreign metal; the stainless appliance was also dissolved in those regions. The authors suggest that the

amount of metallic transfer depends on the specific nature of the contracting surfaces. There are several ways in which its control might be attempted. One simple way is to consider the relative hardness of each of the contracting metals. The effect of the hardness of the tool has been investigated quantitatively. Samples of surgical drivers and screws have been treated to alter their durability, and the amounts of transfer occurring with various combinations have been measured. The authors state that the transfer might be reduced appreciably by increasing the hardness of the drivers or softening the screws. It does not necessarily follow, however, that the smallest electrolytic action will occur when a hard tool is used. Although a hard tool will reduce the metallic transfer, it will cause increased mechanical deformation of the oxide layer on the screw and may thus affect the inert nature of the metal. The authors believe that the metallic transfer could be reduced appreciably if a suitable inert lubricant was used between the tools and the orthopædic components. This might provide a simple solution to the problem and could be especially effective in reducing transfer if used in conjunction with non-slip screwdrivers.

Repair of Defects in the Tendo Achillis.

D. M. BOSWORTH (*J. Bone & Joint Surg.*, January, 1956) states that the repair of defects in the *tendo Achillis*, by replacement with fibrous tissue, is unsatisfactory. Fibrous tissue interposed in the defect has been shown to stretch gradually and to be unable to withstand the stress imposed upon it by the calf muscles. Delayed repair, or repair of an old defect, is performed by use of the raphe of the *tendo Achillis*. It is pointed out that this raphe extends upwards on the posterior surface of the calf muscles three-fifths of the way from the heel to the knee. By vertical incision over this area the *tendo Achillis* and the upward extension of the tendinous raphe are exposed. A one-half inch strip from the central portion of this raphe is incised and freed from above downward, and is left attached to the proximal end of the tendon just above the defect. This provides a section of tendinous tissue from seven to nine inches in length. Closure of the defect left in the calf with interrupted sutures reconstitutes the lower calf muscles and the upper portion of the *tendo Achillis*. The strip of tendon, turned downward, is then passed transversely through the proximal end of the ruptured *tendo Achillis* in order to imbricate it there and to prevent its pulling out. The fibrous tissue interposed between the ends of the damaged tendon should be removed. The strip of tendon is passed transversely through the distal end from behind forwards. The strip is brought upward and is passed transversely again through the proximal end of the *tendo Achillis* and is drawn tight, fixed with one or two chromicized sutures, and brought down and again sutured to itself. The tendon graft, which crosses the defect, does not have sufficient strength to resist the forces imposed by the calf muscles, but merely acts as a bridge of continuity of tendinous tissue of the same texture as the original *tendo Achillis* between the separated ends. The foot is immobilized with plaster in plantar flexion, and no weight-bearing is allowed for six weeks. Marked hypertrophy of the tendinous structure occurs. Full weight-bearing was permitted in the author's patients approximately three months after operation. It can be noted, from the patients in this series, that the tendon eventually returns to essentially its normal size.

Arthrodesis of the Osteoarthritic Hip Joint.

R. WATSON-JONES AND W. C. ROBINSON (*J. Bone & Joint Surg.*, February, 1956) have reviewed 120 patients aged from ten to seventy years, treated for osteoarthritis of the hip joint by intraarticular arthrodesis. Internal fixation was brought about by the use of a nail, usually together with an iliac graft. The hip was immobilized in plaster for not less than four months. Of these 120 patients, there was sound fusion of the joint, proved radiographically, in 94%, there was no mortality, and there was eventual recovery of free movement of the knee joint to the right angle or far beyond in 91·5% of the patients. Almost half of the patients regained normal mobility so that the heel could touch the buttock. Only in eight patients was there less than right-angled flexion. The authors found that there was no residual pain in the back in 64% of the patients. In 36% there was some pain or discomfort. One patient complained that the low back pain was worse than before the operation. Many others reported that the pain in the back had been relieved by the operation. The authors emphasize that these results were gained only from sound fixation of the joint in the mid-position with no rotation, with no more abduction than was needed to correct true shortening, and with no more flexion of the joint than that with which the patient lay on the table. The limb was immobilized in plaster for at least four months after operation. The stiff knee was mobilized by the patient's own exercise without passive stretching, force, or manipulation. The authors have found that after successful arthrodesis of the hip joint, patients can return to every household activity and every recreation including skiing, mountaineering and rock climbing.

Circumduction Fusion of the Spine.

D. M. BOSWORTH (*J. Bone & Joint Surg.*, April, 1956) has operated on 17 patients with mid-line infection or with defects of the spine which prevented a routine surgical approach. To secure ankylosis and to stabilize the spine, it was necessary to construct a fusion of the spine above the defect and extending laterally on the ribs or transverse processes and returning back to the spine below the defect. Twenty-nine operations were performed on these 17 patients in the attempt to secure continuity of the circumduction fusion around the affected spinal areas. In 13 of the patients the fusion was in the thoracic or the thoraco-lumbar areas. These were all patients with tuberculosis of the spine. In four instances the fusion was in the lumbar area; three fusions extended to the sacrum. One of the four patients had tuberculosis of the spine. Three were patients who had severe instability of the spine resulting from wide laminectomy with removal of the articular processes. Of the 13 patients who had circumduction fusion in the thoracic or thoraco-lumbar segments of the spine, solid fusion was secured in 11. The average area covered was that of nine segments. In the lumbar region dependence must be placed on transverse processes instead of ribs for graft contact. Of the four patients operated on, firm bony union was obtained in two. Eleven patients had paraplegia; seven of these totally recovered, two have recovered 75% of function, and one recovered 50% of function. One is still totally paraplegic. The author concludes that a circumduction fusion, when solid, has been shown to be effective in immobilizing the spine and arresting disease. It is again emphasized that in patients with paraplegia due to tuberculosis of the spine the treatment of choice is fusion across the involved area. Wide laminectomy and facetectomy can produce a severely disabling condition and require lateral circumduction fusion to restabilize the spine. Construction of a circumduction fusion may require numerous procedures to secure continuity. Circumduction fusion can succeed, even when covering long areas of the spine, if repeated surgical procedures are accepted by the patient.

Effect of Anticoagulants on Bone Repair.

F. E. STINCHFIELD, B. SANKARAN AND R. SAMILSON (*J. Bone & Joint Surg.*, April, 1956) noted the occurrence of pseudarthroses in four patients who had received anticoagulant therapy for thrombophlebitis immediately after an operation. A controlled investigation, in which experimental animals were used, was undertaken to determine the possibility of there being a causal relationship between anticoagulants and the poor healing of bone. The authors found that when the animals received anticoagulants in the pre-operative period, they showed evidence of delayed union; when the anticoagulants were given in the immediate post-operative period, fibrous union resulted; when heparin or dicoumarol were given one week after the operation, delayed union occurred. The authors believe that there are two possible explanations for the findings of this study; one involves mechanical conditions and the other involves cellular conditions: (i) mechanical; there may be a lack of scaffolding in the form of the fibrin clot upon which the osteoblasts form bone; and (ii) cellular; attributable to the toxic effect of the anticoagulants, there may be a definite diminution in the number of cells at the graft site or there may be an alteration in the normal metabolic process in the bone matrix. The authors stress that one cannot conclude from this study that there will be a failure of union in a patient who has received anticoagulant therapy; they think, however, that the possibility of such an occurrence must be considered.

Medical Societies.

AUSTRALIAN PÆDIATRIC ASSOCIATION.

The annual meeting of the Australian Pædiatric Association was held at the Australian Institute of Anatomy, Canberra, on April 13 to 15, 1956, Dr. Kate Campbell, the President, in the chair.

Annual Report and Financial Statement.

The annual report and financial statement for the preceding twelve months were received and adopted.

Registration of the Association.

The Australian Pædiatric Association was registered under the *Companies Act* of New South Wales during the year 1955-1956. At the annual meeting the members of the Association were officially incorporated in the new Association.

Election of Office-Bearers.

The following office-bearers were elected for the year 1956-1957.

President: Dr. T. Y. Nelson.

Vice-President: Dr. M. Cockburn.

Immediate Past President: Dr. Kate Campbell.

Honorary Secretary: Dr. S. Bellmaine.

Honorary Treasurer: Dr. D. Dey.

Executive Committee: Dr. P. A. Earnshaw (Queensland), Dr. R. Wall (Tasmania), Dr. R. Crisp (Western Australia).

The Next Annual Meeting.

It was decided to hold the next annual meeting of the Association at Canberra in April, 1957.

Cardio-Œsophageal Reflux.

Frieda Plarre (Melbourne) read a paper entitled "Cardio-Œsophageal Reflux" (see page 241).

Russell Howard (Melbourne), in opening the discussion, said that from the surgical viewpoint he wished to emphasize three points. First, œsophagoscopy was necessary in all cases and should be carried out by the surgeon who might be dealing with the patient at a later date if conservative treatment was unsuccessful, and not by an ear, nose and throat surgeon. The investigation should be carried out early in the disease, as it was the only way in which œsophagitis could be diagnosed and it was the only way in which progress could be watched. Dr. Howard said that stricture formation was preceded by œsophagitis. When patients were treated conservatively œsophagitis might subside, but in some it did not and stricture resulted. It was much better for the surgeon to deal with an œsophagitis not responding to conservative management than to be presented with the problem when a stricture was present. When the patient was seen early with œsophagitis not responding to treatment, surgical replacement of the stomach into the abdominal cavity might reduce reflux and allow the œsophagitis to subside. Once an organic stricture was present, surgical excision of the stricture was inevitable, and this was a much more formidable problem. Secondly, Dr. Howard said that he wished to emphasize that conservative treatment, even though adequate, was not always successful. Thirdly, hæmorrhage was sometimes an indication for surgical intervention. Hæmorrhage was not an uncommon complication in the condition, and when severe and persistent called for surgical intervention.

Mostyn Powell (Melbourne) said that he did not agree with Dr. Howard that œsophagitis could not be diagnosed without œsophagoscopy. He considered that hæmorrhage and severe lower thoracic and epigastric pain indicated œsophagitis. Pain was sometimes a very intractable symptom, and in one case after using alkalis and aspirin he had had to resort to the use of a dilute solution of cocaine.

Howard Williams (Melbourne) said that he did not agree that œsophagoscopy was necessary in all of these patients. There was a strong natural tendency for healing to occur in a large number and œsophagoscopy in every case constituted needless interference. He considered that œsophagoscopy was indicated for those children who were not responding to treatment.

Robert Southby (Melbourne) pointed out that the routine nursing of such young infants in the upright position was not without complications. He had observed in some of his patients that after a period of time they did develop deformity of the head, in the nature of a flattening of the vertex.

D. Hamilton (Sydney) asked Dr. Plarre how long after the onset of the condition symptoms of œsophagitis could develop for the first time. He said that he had in his care a girl of twelve years who had presented with symptoms of pain in the epigastrium and vomiting of blood of short duration. Previously she had had mild intermittent vomiting over a period of years. Œsophagitis had been demonstrated by œsophagoscopy and barium meal X-ray examination, and the lesion was not responding to treatment with alkalis and posture.

Kate Campbell (Melbourne) asked Dr. Plarre if she considered that there was a particular constitutional type of infant with the condition. In her experience there were two definite types of children with the disorder: the first was the nervous or dyskinetic type and the second was the hypotonic child with poor general muscle tone.

In reply, Dr. Plarre said that many of the patients were of the nervous, hyperactive type at the time of examination. Occasionally a quiet placid child would show very free reflux. However, it was not possible to assess at intermittent examinations whether the child was primarily of a nervous dyskinetic temperament or whether the symptoms of dyspepsia from which some of the children suffered a good deal were responsible for their irritability and nervousness. In a child with hypotonia and poor general muscle tone, perhaps secondary to some other systemic illness, a mild degree of reflux could sometimes be demonstrated radiologically. She went on to say that the diagnosis of œsophagitis in children was not always a clear and simple problem, for the nature of the underlying pathology was still comparatively unknown. The typical appearance of reflux œsophagitis was sometimes seen in young children. Endoscopically it had a characteristic appearance and the underlying pathological change was that of superficial digestive destruction of the mucosa. However, this typical appearance was only occasionally seen in children with reflux, and other types of mucosal changes could not be explained until further pathological data were available.

Dr. Plarre said that in 1950 Gruenwald in a pathological study of 300 consecutive neonatal deaths found 52 cases of acute œsophagitis. In none of them was any hernia or other anatomical deformity of the hiatal region present. All cases had been studied microscopically and the changes were not those of reflux œsophagitis. It was possible that the type of non-specific œsophagitis referred to could, if perpetuated, cause incompetence of the cardia with reflux in a proportion of cases. Reflux œsophagitis was a subsequent complication of gastric reflux. In conclusion, Dr. Plarre said that in adult surveys, Lodge had shown in one series of 500 unselected hospital autopsies an incidence of 31% of non-specific œsophagitis (in all cases routine microscopic study of the gastro-œsophageal junction was carried out); while Peters in a series of 116 cases of severe œsophagitis, selected from a large range of post-mortem material, found only 30% of cases associated with hiatus herniæ.

Anæmia following Replacement Transfusion in Hæmolytic Disease of the Newborn.

S. E. J. Robertson (Sydney) read a paper entitled "A Study of the Anæmia following Replacement Transfusion in Hæmolytic Disease of the Newborn" (see page 250).

Elizabeth Turner (Melbourne) opened the discussion. She stated that in a series of one hundred cases of exchange transfusion in Melbourne, sixty-five patients developed anæmia requiring blood transfusion. In a few of these cases the patient developed a hypoplastic anæmia with reticulocyte depression. Some patients required more than one blood transfusion. Dr. Turner felt that the anæmia was related to the persistence of antibodies in the infant's serum associated with a positive indirect response to a Coombs test. It seemed, Dr. Turner said, that rhesus antibodies had a direct effect on the bone marrow. In mild cases of this anæmia specific therapy was not required. In Melbourne it was customary to give transfusions to the infants when the hæmoglobin level reached 9·0 grammes *per centum*. Some patients needed up to five transfusions. Dr. Turner stated that the cord hæmoglobin levels in Melbourne averaged 10·6 grammes *per centum*. After exchange transfusion, the average hæmoglobin level was 11·9 grammes *per centum*.

KATE CAMPBELL (Melbourne) asked Dr. Robertson the algebraic sum of the hæmoglobin levels of the combined packed cells and bank blood. In her experience the hæmoglobin level of bank blood was approximately 70%. She further stated that observation of the white cell series in these cases would be most instructive. In one case which she had studied there was depression of leucopoiesis as well as erythropoiesis, indicating general marrow depression.

In reply to Dr. Turner, Dr. Robertson said that only twenty-eight cases of anæmia following exchange transfusion had been studied with serial hæmoglobin estimations. In the remainder of the fifty-eight cases the number of hæmoglobin determinations was too few to be included in the study. Dr. Robertson further stated that he had not seen the picture of hypoplastic anæmia described by Dr. Turner. Bone marrow biopsies had not been performed in his own cases.

In reply to Dr. Campbell, Dr. Robertson said that the hæmoglobin levels in the blood used for exchange transfusions had not been determined. The hæmatocrit levels, however, were between 40% and 60%. Packed cells had been used for only a short period, and the hæmatocrit level of this blood would be given in a further report.

Febrile Convulsions in Infants and Childhood.

WILFRED CARY (Sydney) read a paper entitled "Febrile Convulsions in Infancy and Childhood" (see page 254).

D. HAMILTON (Sydney), in opening the discussion, said that he considered that in general the prognosis of febrile convulsions was good. However, he would qualify this and would make two points. These were first, that he did not consider that a follow-up period of ten years was sufficiently long in a condition such as epilepsy and that the patients would have to be followed for a much longer term before the final results were known. Secondly, in idiopathic epilepsy the outlook was also good if the seizures were controlled by anticonvulsive therapy. The abnormal electroencephalographic findings disappeared after a variable number of years in the case of many children whose fits had been controlled. The outlook was not good when organic brain damage was present or if the seizures could not be controlled by adequate treatment.

Dr. Hamilton said that two points were of importance in considering whether the child suffering from febrile convulsions should be treated. First, was the child likely to become an epileptic? In determining this one had to be guided by the family history, the electroencephalographic findings and evidence of brain damage. When there was a family history of convulsions, when frankly dysrhythmic changes were present in the electroencephalogram or when there was evidence of brain damage, he thought treatment should be instituted, and he would be hesitant about giving a prognosis in such cases. Secondly, he said that it was open to question whether febrile convulsions should be treated in an attempt to prevent further febrile convulsions. Lennox based her treatment on the severity of the convulsion, the age of the patient and a family history of epilepsy. Dr. Hamilton based his opinion also on those factors, and thought that treatment was justified if the patient was less than twelve months of age or older than three years when the first convulsion occurred. In a child who had had two convulsions or when the electroencephalographic pattern was abnormal or when organic brain damage was present, he treated the patient for a period of two to three years.

ROBERT SOUTHBY (Melbourne) asked whether febrile convulsions were considered to be due to the actual fever present or whether they were thought to result from toxæmia due to infection. He also asked whether it was known why in some virus infections such as measles, convulsions were common, whereas in others, such as poliomyelitis, they were very uncommon.

S. E. J. ROBERTSON (Sydney) asked how many of the six children who subsequently developed epilepsy had received anticonvulsant therapy.

S. W. WILLIAMS (Melbourne) asked why children with fever had convulsions if they were not epileptic.

In replying to questions, Dr. Cary said that the reason why a ten-year follow-up period was chosen was to enable the study to be carried out in a children's hospital.

To Dr. Southby Dr. Cary said that he was unable to answer the question of the variability in the incidence of convulsions in virus infection. As far as the cause of convulsions was concerned, experimental work had shown that in young kittens convulsions could be produced by rapidly increasing their temperature, whereas in older kittens and cats convulsions did not occur under the same conditions. It was also found that when the temperature was gradually raised to the same degree, convulsions did not occur.

To Dr. Robertson, Dr. Cary replied that none of the children who subsequently developed epilepsy had received treatment after their febrile convulsions.

To Dr. S. Williams, Dr. Cary said that he considered that every individual had a threshold at which he would have convulsions, and this varied considerably from person to person.

Exchange Transfusion of Rhesus-Positive Blood in Hæmolytic Disease of the Newborn.

S. E. L. STENING (Sydney) read a paper entitled "The Use of Exchange Rhesus Positive Blood in Transfusion for Hæmolytic Disease of the Newborn" (see page 246).

ELIZABETH TURNER (Melbourne), in opening the discussion, said that the treatment of the condition depended to some extent on the particular theory of ætiology of kernicterus to which the operator adhered. She believed that kernicterus had a direct relationship to the level of serum bilirubin and particularly to the level of indirect bilirubin. Rhesus-positive cells introduced into the circulation of the infants were rapidly hæmolysed and there was a resulting increase in circulating bilirubin. That necessitated further exchange transfusions and so enhanced the risks to the child. Dr. Turner said that she did not agree with Dr. Stening that rhesus-positive cells entering the circulation were not harmful. Wiener had shown that that procedure could produce a frank hæmolytic reaction. Giblett, using chromium-tagged cells, had shown that whereas the normal survival time of transfused cells was over fifty days, the survival time of rhesus-negative cells introduced into these children was approximately thirty-six days, and rhesus-positive cells were almost completely destroyed within twenty-four hours. In conclusion, Dr. Turner thanked Dr. Stening for his most stimulating paper, but said that she would like to study the paper in some detail before commenting further.

FELIX ARDEN (Brisbane) commented that the reason given why the infants under discussion did not react adversely to transfused rhesus-positive cells appeared logical. It was possible that large quantities of antibody were already attached to brain and liver cells at the time of the transfusion. He asked Dr. Stening if he thought that the increased number of stillbirths in recent years was due to the changing attitude to induction of labour in rhesus incompatibility. Previously, labour was often induced at thirty-six weeks, whereas the modern approach was to allow pregnancy to proceed to term.

D. HAMILTON (Sydney) asked Dr. Stening how prolonged and how intense was the jaundice in the infants under discussion before and after transfusion with rhesus-positive cells. He thought that this was important as it might help to define whether or not the level of serum bilirubin was important in the development of kernicterus.

JOHN PERRY (Melbourne) said that he, like Dr. Hamilton, was interested to know what part serum bilirubin had in the development of kernicterus in the infants under discussion. He said that in his observations of infants with jaundice due to infective hepatitis and congenital obliteration of the bile ducts, high serum levels of bilirubin had been encountered without eventual autopsy evidence of kernicterus. Dr. Perry asked Dr. Stening whether serum levels of total, direct and indirect bilirubin were estimated routinely in infants in this series.

KATE CAMPBELL (Melbourne) thought that, apart from the level of serum bilirubin, other factors had to be considered in these infants, and not the least important were the "cells themselves". She referred to the Scandinavian workers who showed that the levels of bilirubin in the cerebro-spinal fluid did not always parallel levels in the blood, and that anoxia rendered the blood-brain barrier more permeable to bilirubin. She thought that the cells of the central nervous system, if damaged, for example, by hypoxia, might be more prone to further damage by bilirubin. However, she was convinced that the level of bilirubin in the serum was important, as kernicterus in premature infants could be prevented by keeping the serum bilirubin level low. Dr. Campbell said that in this series it was too early to be sure that the infants were normal, as the period of follow up was not of sufficient length. She thought that further observation was necessary to exclude such things as deafness, which could not be assessed at the present stage.

In replying to Dr. Turner, Dr. Stening said that the observations in the series did not support the views of

Giblett and Wiener, as no adverse effects had been encountered which could be attributed to the use of rhesus-positive cells in exchange transfusions given to the infants. He told Dr. Arden that in this series the majority of infants weighed six pounds or less. There had been no significant reduction in the numbers of labours induced, though induction was not encouraged. He said that one of the ideas behind the use of rhesus-positive blood in these cases was to neutralize circulating antibody and perhaps attract antibody, already attached to brain and liver cells, to the circulation where it could act freely on the circulating positive cells.

To Dr. Hamilton he said that the intensity and duration of the jaundice varied considerably. In the mild cases it was common for jaundice to clear in one to two days, whereas in the severe ones it had persisted for periods of seven or eight days or longer. The longest period was approximately three weeks in an infant who had a mild "inspissated bile" syndrome.

Dr. Stening answered Dr. Perry's question by saying that the level of total serum bilirubin only was estimated. Direct and indirect levels were not estimated.

To Dr. Campbell, Dr. Stening said that, apart from the factors which had already been considered, he wondered whether or not there might be a genetic factor involved as well. He said that he had observed families in which more than one child had been affected and in which the condition had appeared in a mild form; in other families severe forms, like hydrops, had recurred, while in several families kernicterus affecting more than one child had been encountered.

A Case of Aminoaciduria with Other Biochemical Abnormalities.

David Jackson (Brisbane) presented a case of aminoaciduria with other biochemical abnormalities (see page 256).

John Perry (Melbourne), in opening the discussion, said that, initially, aminoaciduria had been regarded as a disease entity, but it was now known to be a symptom and a feature of diseases such as cystine storage disease and Kinnear-Wilson's disease. Physiologically, aminoaciduria might be present in newborn infants, and temporarily it was seen in scurvy, non-resistant rickets (vitamin *D* deficiency rickets), lead poisoning, subacute nephritis and hepatitis. Aminoaciduria was produced in two ways. In the first a high serum aminoacid level was present, as, for example, in hepatitis due to failure of deamination. Here the kidneys could not cope with the aminoacid load presented to them and aminoaciduria resulted. Secondly, aminoaciduria was associated with a normal serum aminoacid level. This implied a renal tubular defect. Energy was required in the mechanism of resorption of aminoacids by the renal tubular cells. This energy was supplied by glucose. Thus any process which interfered with intracellular glucose metabolism might prevent aminoacid resorption. It was known that galactose could prevent the uptake of glucose by cells. Dr. Perry queried whether in Dr. Jackson's case there was deficient uptake of glucose in the renal tubular cells and whether the energy necessary for the resorption of aminoacids was thus deficient. In support of such a theory, Dr. Perry directed attention to the disappearance of aminoaciduria in vitamin *D* deficient (non-resistant) rickets when the disease was cured.

Douglas Galbraith (Melbourne) asked if there were any bone changes in Dr. Chalk's case. He said that there were two distinct mechanisms causing the bone changes in renal tubular disease. The first was the loss of phosphate with consequent lowering of the calcium-phosphate solubility product; this resulted in failure to precipitate calcium phosphate. The second and more interesting mechanism was the occurrence of acidosis with consequent actual loss of calcium base. This had been considered to be due to failure of the proximal tubules to reabsorb sodium bicarbonate which led to accumulation of bicarbonate in the distal tubules with consequent inhibition of ammonia formation. However, there was still doubt about this mechanism. Dr. Galbraith was glad to note that both Dr. Chalk and Dr. Jackson had used potassium as well as sodium salts as there was often a lowering of the intracellular potassium content. The loss of potassium when alkalis and glucose were given together was important. In one reported instance a patient on alkali therapy had died during the making of a glucose tolerance test, probably from potassium loss. Dr. Galbraith commended the work of the metabolic unit of the Royal National Orthopædic Hospital, London, in such studies, and said that they had found sodium and potassium bicarbonate to bring about more rapid healing of bone than the citrate mixtures given by Dr. Chalk and Dr. Jackson. The citrate mixtures had originally been used as a means of providing oral base without making the gut alkaline, as the alkalinity was thought to hinder calcium absorption. Present evidence was against this conception.

Anomalies of the Prepuce of the Clitoris.

Robert Vines (Sydney) read a paper entitled "Multiple Congenital Anomalies Associated with Hypertrophy of the Prepuce of the Clitoris".

E. Stuckey (Sydney) said that Dr. Vines's photograph unfortunately could not show the mobility and looseness of the structures, which were comprised solely of skin and subcutaneous tissue. He said that clitoral tissue could not be palpated.

Peter Jones (Melbourne) asked if malposition *in utero* might be the cause of the unusual rib compression in the second case, particularly in view of the talipes in another case and the depressed bridge of the nose. Extended legs might conceivably be the factor producing the chest and nasal deformity.

Kate Campbell (Melbourne) commented on the increased number of fœtal abnormalities seen in Melbourne over the previous twelve months. These abnormalities were of unusual types. Dr. Campbell stated that Dr. Vines had been able to show that the noxious fœtal influence in his cases acted between the second and fifth months. With the large number of chemical substances used at the present time, it was possible, Dr. Campbell said, that some of them might be noxious to the developing fœtus. She stressed the view that careful observation might support this hypothesis.

In reply, Dr. Vines stated that while the types of talipes present were compatible with uterine pressure, there was nothing to suggest that pressure due to extended legs produced the chest or facial deformity in the cases presented.

Addison's Disease in Infancy.

Alan Williams (Melbourne), in presenting his paper, said that Addison's disease occurred not only in infants with the adreno-genital syndrome, but in infants whose adrenal glands were diseased or hypoplastic. In support of this statement he presented the salient clinical features and autopsy findings in three cases in which clinical features suggestive of Addison's disease were associated with the demonstration at autopsy of diseased or hypoplastic adrenals.

The first infant was admitted to hospital when aged thirteen months in December, 1948, in a moribund condition. She had thriven from birth until her present illness which consisted of vomiting for thirty-six hours. The infant died one hour after admission to hospital and at autopsy the only abnormality found was the presence of small adrenal glands which contained areas of calcification. Microscopically the adrenal cortex had been largely replaced by amorphous material and fibrous tissue, in which calcium and hæmosiderin were present.

The second infant, a male baby, was admitted to the Royal Children's Hospital, Melbourne, aged four weeks, in July, 1948. When aged two weeks, the baby had commenced to vomit and became dehydrated. The only abnormality found on clinical examination was emaciation. Ten days after admission the baby suddenly became dehydrated. This occurred in the absence of vomiting and diarrhœa. Despite intravenous therapy, hydration could not be maintained and death occurred suddenly eighteen days after admission. At autopsy extremely small adrenal glands were found. Histologically the adrenal cortex was well differentiated and separated from well-formed medullary tissue by a thin layer of fibrous tissue, in which calcium and hæmosiderin were present.

In the third case, the patient, a female baby, aged two days on admission to hospital, was lethargic, vomited persistently and refused feedings. Investigations revealed no cause for this state. Two weeks after admission dehydration became pronounced and the skin was noted to be grey. Acute bronchopneumonia caused death shortly afterwards. At autopsy, as well as extensive bronchopneumonia, hypoplastic adrenals were found. In the adrenal glands a well-formed definitive cortex was situated immediately adjacent to medullary tissue. No fœtal zone or condensation of stroma representing this zone could be found.

Dr. Williams stated that of the seven similar cases reported in the literature, there had in six been hypoplastic adrenals, a condition which was usually associated with anencephaly. Hæmorrhagic destruction of the adrenal glands, such as occurred in the first case and also partly in the second case, presumably occurred at birth. In support of this Dr. Williams presented a further case history of an infant with cerebral palsy, presumably following a difficult delivery, who died suddenly when aged three months. A large portion of that infant's adrenals had likewise been destroyed by hæmorrhage. Fibrous tissue replacement with hæmosiderin pigment and calcification was found at autopsy. In sections of all these adrenal glands Dr. Williams could find no evidence of regeneration, which seemed surprising in view of experimental work on this subject.

M. J. ROBINSON (Melbourne) presented the clinical details of an infant with Addison's disease who had responded to treatment with cortisone and salt. This infant was aged ten weeks and weighed seven pounds five ounces when admitted to hospital. His birth weight was seven pounds seven ounces. He was dehydrated on admission and pigmentation was noticed. The possibility of Addison's disease was suggested by serum electrolyte levels, the serum sodium being 120 milliequivalents per litre and potassium nine milliequivalents. Fasting blood sugar levels were low. Analysis of urine showed that a twenty-four-hour output of 17-hydroxysteroids was 0·045 milligramme and 17-ketosteroids was 0·7 milligramme. The serum 17-hydroxysteroid level was less than two micrograms per 100 millilitres. During the period of observation and investigation the baby had not gained weight and had remained slightly dehydrated throughout. Treatment with 25 milligrammes of cortisone given orally twice a day resulted in no improvement until sodium chloride was added to the feedings and a dramatic increase in weight occurred. This improvement had been maintained; there was no sign of œdema, glycosuria or elevation of blood pressure and the baby was active and had a much better colour. Serum electrolyte levels prior to the baby's discharge from hospital were normal. When he was last seen at the age of seven months, his weight was seven pounds and development had been normal in all respects. Cortisone and salt therapy had been continued, but in reduced quantities. Dr. Robinson thought that the features of failure to gain weight, dehydration despite theoretically adequate fluid intake, and skin pigmentation should suggest a diagnosis of Addison's disease. The diagnosis could be confirmed by demonstration of a typical electrolyte pattern in the serum, and by a low 17-hydroxysteroid level in the urine. Final proof of the correct diagnosis was shown by the disappearance of signs and symptoms with substitution therapy. Treatment of an Addisonian crisis consisted of administering adequate fluid, sodium chloride and glucose intravenously, together with cortisone or cortisone and DOCA. In maintenance therapy, Dr. Robinson suggested that cortisone with its hyperglycæmic action was preferable to DOCA. He said that with this mode of treatment additional salt was usually necessary.

ROBERT VINES (Sydney) opened the discussion. He said that at the Royal Alexandra Hospital in Sydney they had not had experience with the condition in this age group either clinically or pathologically. He thought it was remarkable that one unit should find four infants with Addison's disease. He considered that the documentation of the treated case in this series was the most convincing in the literature. He pointed out the dangers of making a diagnosis of Addison's disease in this age group as the two main methods of presentation were either with a severe illness of short duration and sudden death, or with a more insidious illness and failure to thrive. Such symptomatology could result from many causes, and there was always the danger of endeavouring to label such cases as adrenocortical in origin without sufficient confirmatory evidence.

Dr. Vines said that interpretation of results of investigations was difficult in this type of case in infancy, and the diagnosis of many cases in the literature depended considerably on serum electrolyte levels and on the quantity of steroids excreted in the urine. A low sodium level was straightforward and common to many states, but to accept a diagnosis of hyperkalæmia the level of serum potassium had to be very high, as normal serum potassium levels in normal infants were usually high. As far as the 17-hydroxysteroids were concerned, Dr. Vines said that he thought the urinary levels were in all probability usually a satisfactory mirror of serum levels. However, the normal range of 17-hydroxycorticoids in both blood and urine was not firmly established as yet in this age group.

In considering treatment of cases of infantile Addison's disease reported in the literature, Dr. Vines said that he was surprised at the large doses of DOCA used, often as much as two milligrammes of DOCA for small infants, and this dosage was often sufficient to control Addison's disease in adults.

In conclusion, Dr. Vines said that the recently available fluorohydrocortisone might assist accurate diagnosis while treatment was being given, by enabling ACTH response of eosinophile cells and steroids to be observed during the continuation of adequate treatment given on suspicion of the presence of hypoadrenocorticism.

STANLEY WILLIAMS (Melbourne) asked Dr. Robinson whether or not this was a self-limiting condition in infancy and would it be possible at a later date to discontinue treatment.

R. GODFREY (Perth) commented that recently in Western Australia they had treated an infant suffering from electrolyte depletion and dehydration, who had proved to be a female pseudohermaphrodite, although the external genitalia were normal in appearance.

KATE CAMPBELL (Melbourne) asked Dr. Alan Williams whether there was a history of difficult breech delivery in any of the infants he had described. She said that suprarenal hæmorrhage could result from manipulations in delivery and that she had had personal experience of one such infant who, following difficult breech delivery, was shown to have radiological evidence of adrenal calcification at the age of three months. She also asked Dr. Williams if he had encountered similar pathological features in the adrenals of infants who died in an eczematous crisis.

In reply to Dr. Stanley Williams, Dr. Robinson said that Jaudin (1948) presented a series of cases with clinical and biochemical diagnoses of Addison's disease in infancy. These infants responded well to treatment with DOCA, and after periods varying from five to twenty-two months therapy was discontinued without harmful effect. He said that cessation of treatment was not being considered in his case at the present time.

In reply to Dr. Campbell, Dr. Alan Williams said that, of the two infants whom he had examined and who had had adrenals destroyed by hæmorrhage, the first had had a normal delivery and the second had had a difficult forceps delivery. He had examined the adrenals of a large number of infants and children who had died from various causes, and these included a small number who died in an eczematous crisis. In none had he found changes resembling those seen in the infants reported.

Investigation of Steatorrhœa in Childhood.

In presenting a paper on the investigation of steatorrhœa in childhood, DR. C. ANDERSON (Melbourne) said that three years previously she had delivered a paper on the subject of cœliac disease, discussing at that time work done overseas. During the last three years at the Clinical Research Unit of the Royal Children's Hospital, the study of gastrointestinal disorders in childhood associated with steatorrhœa had been continued. Clinical material had been referred by the hospital staff and others and this material had been studied from many aspects. The studies most closely related to clinical pædiatric practice had been chosen as the substance of the present paper.

Dr. Anderson said that the term steatorrhœa was used very broadly in clinical pædiatric medicine. It seemed in general to be applied to the passage of large pale stools by the patient at some stage, but it also seemed that the term was used synonymously with such terms as cœliac syndrome, starch intolerance and fat intolerance. However, in her paper the term was defined within narrow limits—steatorrhœa meant the passage of stools containing an excessive amount of fat, as determined by a fat balance determination. Pale stools were not necessarily fatty. Colour depended on many factors, such as the rate of passage through the gut, the oxidation or reduction of bile pigments and the flora of the gut. Steatorrhœa did not always mean diarrhœa and abnormally fatty stools might at times be formed or even constipated. Although a pale stool might contain excess fat, it might at the same time contain excess protein and carbohydrate. These substances did not make their presence obvious macroscopically as did fat, and therefore fat was very apt to be referred to as the most important abnormal constituent of the stool. An instance of this was seen in the history of treatment of cœliac disease, in which former dietary measures had been aimed at reducing only the fat in the stools.

Absorption into the blood-stream of ingested food products was highly efficient, and over 90% of fat, protein and carbohydrate was absorbed by the normally functioning bowel.

Maximal absorption probably depended on three factors, adequate digestion by enzymes, an efficient and adequate absorbing surface and normal motility patterns. Therefore, malabsorption resulting in steatorrhœa might occur from a number of causes, and might be present temporarily, if looked for, in many gastro-intestinal upsets. However, in the cases described malabsorption had been present for long enough to impair health and nutrition.

Fat appeared in the stool in two forms, undigested or neutral fat, and digested or split fat, depending on the presence of adequate enzymes and bile. The former appeared as droplets of oil and the latter as fatty acid crystals or soaps.

A personal observation of the stool both macroscopically and microscopically was important, but by no means diagnostic. Stool appearance could vary greatly, and perhaps the only two features which could be said to be anything more than suggestive were the observation of oily matter (like melted butter) in the stool macroscopically and the appearance microscopically of numerous fat globules. The former was an extremely important point in the history if it had been noticed by the mother. The latter was useful as a screening test which was easily made. A simple examination of a small portion of fæces under the microscope, even without any staining procedure, was sufficient, and Dr. Anderson showed a slide illustrating the fat droplets in a fæcal specimen. The fat droplets were easily seen, but should, she stated, be present in large numbers to be significant; such an examination was to be recommended as an easy office procedure. Fatty acids and soaps, although easily identified, could not be assessed quantitatively by this method. They were present normally in fæces and might be very obvious in a baby's stool without being present in abnormal quantity.

Fat globules were seen in conditions in which digestion of fat was incomplete, such as fibrocystic disease of the pancreas, or in which the passage of food through the gut was hurried, as in acute diarrhœa, or in the absence of bile, as in obstructive jaundice. Fat droplets were not usually seen in any great numbers in cœliac disease, in which the digestion of fat was complete, but the defect was one of absorption. Therefore microscopic examination of the stool was of little value in steatorrhœa from malabsorption, but of value in steatorrhœa from maldigestion. Clinically it was found that this examination was of the greatest value in the group of babies and young children with resistant chest infection who were suspected of suffering from fibrocystic disease of the pancreas.

Steatorrhœa had been demonstrated most satisfactorily by a fat balance study carried out over a period of three to eight days. In all cases referred to in the study a fat balance estimation was made. The unreliability of a single estimation of fat in one stool was then illustrated by reference to studies of Payne, and that method was compared with the balance method.

Dr. Anderson explained that simple laboratory methods were now available for the estimation of fat in stools. Ward collection of specimens remained a difficulty, but it seemed desirable that hospitals for sick children should make provision for a small section where metabolic studies involving balance work could be carried out, as there were quite a sufficient number of diseases in which the accurate collection of urine or fæces over a number of days was important for precise diagnosis.

Efforts were continually being made by various workers to short cut the necessity of a fat balance, by using some other short-term absorption test to assess the disposal of ingested food. The mere multiplicity of these tests indicated their unreliability. They included the glucose tolerance test, vitamin *A* absorption test, the plotting of an aminoacid curve and chylomicrography. Dr. Anderson said that all these were tried in her study, but had been discarded as giving unreliable evidence of malabsorption in many cases. Their use often meant the infliction of needless trauma and the waste of laboratory time for an unreliable result.

In summary, steatorrhœa was demonstrated by fat balance estimation and the type of fat by microscopic examination, no chemical estimation of split and unsplit fat being necessary. The presence or absence of pancreatic enzymes was best demonstrated by duodenal intubation, and there again other tests had been used to try to effect a short cut—tests such as estimation of stool trypsin, the antithrombin test and chylomicrography. So far none of these had given results as consistent as intubation.

The cases which had been referred for investigation and diagnosis were then discussed by Dr. Anderson. She said that they comprised a very mixed clinical group and it was difficult to generalize regarding their symptomatology, but the patients all had some gastro-intestinal upset suspected of being associated with steatorrhœa.

In each case a detailed clinical history had been obtained. Special attention was paid to such points as duration and continuity of symptoms, age of onset of symptoms, family history of similar symptoms, and social and emotional surroundings of the child in the home and elsewhere. The last-mentioned information was obtained by interviews with the mother and observations of the child, and in some cases by a home and school visit by an experienced social worker.

Investigations included physical examination, microscopic examination of the stool, estimation of the fat balance and duodenal intubation as well as other tests relevant to each case.

One hundred and sixteen cases had been investigated by fat balance determination and 78 patients showed steatorrhœa. Of the 78 patients, 25 were found to be suffering from true cœliac disease or to manifest wheat-gluten intolerance; 30 were suffering from fibrocystic disease of the pancreas; and 14 manifested steatorrhœa due to a variety of causes.

The number of cases of cœliac disease, compared with those of fibrocystic disease of the pancreas, did not represent the true difference in incidence of these diseases, because all patients with cœliac disease coming into the hospital had been investigated, but only 39 of 64 with fibrocystic disease of the pancreas.

Dr. Anderson then discussed true cœliac disease or wheat-gluten intolerance and drew attention to the constancy of the clinical pattern of illness. She said that the term wheat-gluten intolerance had been coined to try to overcome some of the difficulties of terminology, and to try to separate the group as a small discrete entity from the condition usually included under the term cœliac syndrome. The latter term was used, particularly in the American literature, to include almost any child who showed a persistent or intermittent bowel disturbance with some interruption of normal growth and progress, its exact meaning varying with different workers. The term cœliac syndrome should probably be abandoned. These patients should not be grouped together into a confused syndrome, because after the taking of a careful history and physical examination with the addition of only simple investigations, a diagnosis could usually be made with moderate certainty and further investigation made for confirmation along particular lines.

Gee's original description of true cœliac disease remained the most accurate and embracing. He described the clinical story of the young child who after a normal babyhood insidiously failed to thrive after the weaning period, with a slow but steady development of anorexia, weight loss, temperamental change, large pale stools, abdominal distension and anæmia. These features had been seen constantly in the twenty-five children in Dr. Anderson's series. Twelve were male and thirteen female. One child had died. Sixteen patients had presented for diagnosis between the ages of ten months and two years, six between two and four years, and three over four years, with a range of ten months to five and a half years. In all cases the symptoms had been present for over two months and in fourteen cases between two and six months.

Twenty-three patients passed large, loose, pale motions, one patient was constipated, one had motions normal in consistency but pale, and two presented with severe diarrhœa with dehydration. In all cases obvious abdominal distension was present. Twenty of the children were temperamentally difficult, many showing depressive features. None had shown such characteristics before the onset of other symptoms and all lost the difficulties after treatment. In no case was there a family history of other known cases of the disease, nor of gastro-intestinal disorders with diarrhœa.

Investigations showed that steatorrhœa was present in all cases, the average fat absorption being 77% with a range of 52% to 89%. In all cases duodenal intubation revealed the presence of normal amounts of trypsin, lipase and amylase for the age. Barium meal X-ray examination showed the anatomical arrangement of the bowel to be normal in 24 cases, and in 23 of them there was the "barred" dilated pattern of the small bowel mucosa, considered consistent with the diagnosis of cœliac disease. In one case it was thought that a normal small bowel pattern was present and in one case no barium meal was given. Blood examination showed that only twelve patients had a hæmoglobin value below 80%, the anæmia being of a hypochromic microcytic type, except in one case in which a macrocytic anæmia was present. Some other features of the cases included the fact that 23 of the

children were of a very blond colouring, and there was a history of allergy in only seven instances. One child had eczema. In only one child could the appetite be described as good. The number of 25 in three years compared with Sheldon's 74 in nine years at Great Ormond Street, and 30 in three years quoted by French *et alii* at the Birmingham Children's Hospital, England. The two groups of workers had applied the same rigid criteria to their diagnosis of the condition as had been applied in the present series.

Two of the patients presenting when over four years of age were first considered to be suffering from anæmia resistant to iron therapy. However, both had abdominal distension and steatorrhœa, although the bowel habit of one was considered normal.

Dr. Anderson then referred briefly to the cases of fibrocystic disease of the pancreas. She said that with an increasing knowledge and experience of that disease a definite clinical pattern was found to exist, a nutritional and bowel disturbance associated with persistent or recurrent chest infection, with at least some features present from birth.

Features present in the clinical history and preliminary investigations such as microscopic examination of the stool separated the group very definitely from true cœliac disease, and the need for further investigation to differentiate the two seldom arose. The more difficult diagnosis was between fibrocystic disease of the pancreas and other conditions characterized by persistent or recurrent chest infections.

Dr. Anderson said that 39 cases of fibrocystic disease of the pancreas had been investigated during the previous three years; nineteen of the patients were female and twenty male. Twenty-eight of the patients were still alive, ten of them being under four years of age, eleven between four and eight years, and seven between eight and twelve years. The patients who died were all under two and a half years of age.

In ten families there were other cases of the disease; three of the patients were only children, and in five families there was a history of stillbirth or miscarriage. In twenty-eight of the cases a diagnosis was made when the children were under four years of age, but eleven patients were over four years before the diagnosis was considered. In most of the latter the diagnosis should probably have been made earlier, but in some instances nutrition had remained remarkably good and chest infection had been minimal. Seven patients had shown no evidence of persistent chest infection before diagnosis, but all their stools contained numerous fat globules and there was a history of oily matter oozing from the stool.

In summarizing the investigations of the cases of fibrocystic disease of the pancreas, Dr. Anderson stated that in 38 cases numerous fat globules were present in the stools. The average fat absorption was 57%, the range being 19% to 96%. In one case there was normal fat absorption with the presence of reduced pancreatic enzymes. In the other 38 cases no pancreatic enzymes were present in the duodenal fluid. *Staphylococcus aureus* was grown from the cough swab in 29 cases, *Bacterium coli* from two cases, *Proteus vulgaris* from two cases, *Bacillus pyocyaneus* from one, and no probable pathogenic organisms from four cases at one examination. X-ray appearances of the chest were abnormal in 35 cases, but within normal limits in four. The child showing decreased enzymes died after the typical chest illness, and the diagnosis was confirmed at post-mortem examination. Two other members of this family had also died of the disease, and one boy, aged fifteen years, was still living and known to have reduced enzymes.

The 14 patients who had steatorrhœa but did not fit into the two main groups were a heterogeneous collection, and in most cases the steatorrhœa was incidental and its presence was not essential to the diagnosis. The group included five patients in whom steatorrhœa was associated with bowel infection or prolonged upper respiratory infection, three in whom it was associated with chronic chest infections, and two in whom it was associated with non-icteric hepatitis; one case was associated with ulcerative colitis, one with malrotation of the gut, one with chronic duodenal obstruction and stagnation, and one with chronic urinary infection (the subject in that instance being a baby).

Finally, Dr. Anderson referred briefly to the 38 patients who were not shown by fat balance estimation to have steatorrhœa. Ten of them were babies with resistant chest infection. In that group microscopic examination of the stools, as well as the chylomicrograph, was useful and possibly circumvented duodenal intubation. Six patients had subacute or recurrent diarrhœa with pale stools, and three of them were shown to have salmonella bowel infection; in two *Giardia lamblia* was found, and one patient had a chronic upper respiratory tract infection.

Twenty-two of the 38 children were referred as cases of fat intolerance. They in general had attacks of vomiting and abdominal pain with the passage of pale stools. However, in all symptoms were intermittent, nutrition was average or good and there was no abdominal distension. In fifteen children the clinical history revealed the presence of obvious emotional difficulties in the environment. This group was not discussed in full by Dr. Anderson as further study was contemplated.

In summarizing her remarks, Dr. Anderson said that she had tried to indicate the most reliable methods of investigation of patients suspected of suffering from steatorrhœa and the range of clinical material which had been seen during the investigation of a series of such children. A carefully taken clinical and social history, with physical examination revealing some interference with nutrition and some abdominal distension, would usually indicate which cases should be more fully investigated. In many cases the actual diagnosis would be fairly definite at that stage with perhaps the addition of microscopic examination of the stool. Further investigation was then planned, usually to confirm the already suspected diagnosis. In doubtful cases a further period of observation might be used.

D. HAMILTON (Sydney) asked Dr. Anderson whether hypochlorhydria or achlorhydria was evident in the group of children with diarrhœa of unknown ætiology. He said that he had treated with hydrochloric acid a number of children suffering intermittent attacks of diarrhœa with variable results. The group who seemed to respond to this regime were those who passed frequent stools with undigested food, but remained well nourished. He was surprised that hypochlorhydria or achlorhydria did not figure in this series as an ætiological factor.

STANLEY WILLIAMS (Melbourne) asked Dr. Anderson whether too many children were referred for special investigation. He wondered if further screening by the physician in charge of the patient was indicated before such children were referred for extensive investigation.

FELIX ARDEN (Brisbane) asked Dr. Anderson why some children with cœliac disease could apparently tolerate gluten for a period of twelve to eighteen months without adverse effects and then develop symptoms of the disease at the age of two or two and a half years. He also wished to know if a child with cœliac disease after a period of treatment with a gluten-free diet later lost intolerance to gluten.

S. STENING (Sydney) had seen many infants and children suffering from gastro-intestinal allergy, especially to milk, and such children often showed emotional disturbances. He wondered if in some of Dr. Anderson's undiagnosed group of patients allergy was a factor in producing the gastro-intestinal upset. A proportion of this allergic group had hypochlorhydria or achlorhydria.

HOWARD WILLIAMS (Melbourne) said that he thought one point should be emphasized. This was the essential need to have a small number of beds in all large hospitals where metabolic problems could be investigated. These beds of necessity had to be separate from general ward beds where it was impossible to carry out balance studies.

KATE CAMPBELL (Melbourne) asked Dr. Anderson why cœliac disease was more common in England and Australia than it was in America. She wondered whether it might be due to the "hardness" of the wheat and the actual percentage content of gluten in the flour. She also asked whether Dr. Anderson thought that some of the children with recurrent bouts of illness characterized by the passage of pale stools were presenting symptoms of the pre-migrainous state. Dr. Campbell was interested to know how many children suffering from fibrocystic disease of the pancreas first presented with asthma.

In reply to questions, Dr. Anderson told Dr. Hamilton that in her series routine test meal examinations were not carried out. The wide variation in levels of hydrochloric acid in normal infants and children made it difficult to interpret results of the test in any particular child. Dr. Anderson did not want to discuss at that stage the children who constituted the "undiagnosed group", but after further investigations and observations a discussion would be of interest.

To Dr. Stanley Williams, Dr. Anderson said that she had been grateful for the large number of children referred for investigation as it gave the opportunity for study of a number of different types of intestinal disturbance. However, in determining which children required extensive

investigation in clinical practice, she considered that a detailed clinical history and thorough physical examination, combined with simple screening tests, such as microscopy of the stool and, in doubtful cases, observation for a period, usually gave sufficient evidence to enable one to decide.

To Dr. Arden, Dr. Anderson said that intolerance to gluten did seem to vary both in the individual child and at different stages of life; moreover, the severity of symptoms increased or decreased when other factors such as infection or poor dietary intake were in evidence. However, a very careful analysis of the clinical history and perhaps the weight chart often revealed some upset at an earlier stage than was obvious. She said that it had been stated in the past that children with cœliac disease recovered in later childhood, but recent follow-up studies in England of children tested with former diets showed that this was not true. Whether children treated with a gluten-free diet would eventually lose their intolerance was not known at present because the follow-up period was limited.

To Dr. Campbell, Dr. Anderson said that it was very difficult to compare figures of frequency of cœliac disease in different countries, as the basis for diagnosis was not the same in all centres. At Great Ormond Street and Birmingham a diagnosis was made of the children's condition on the same criteria as at the Royal Children's Hospital, Melbourne, and from published figures it seemed that the incidence of the disease was similar in the three centres. In America the criteria for diagnosis in some centres did not seem to be as rigid, and therefore the figures were not comparable. She said that the gluten content of wheat probably was an important factor, but she was unable to answer the question with any definite observations. As far as the "undiagnosed group" of cases was concerned, Dr. Anderson could give no data as to what number would eventually be classified as allergic, emotional, migrainous *et cetera* until further studies were made. None of the patients suffering from fibrocystic disease of the pancreas in her series had originally presented with asthma.

The Management of Portal Hypertension in Childhood.

RUSSELL HOWARD (Melbourne), in presenting a paper on the management of portal hypertension in childhood, said that he would deal only with those aspects of the condition which related to investigation and surgical treatment. He emphasized that his own experience had been adequate to enable him to form impressions but not definite conclusions. He said that there were two main types of portal hypertension, one due to intrahepatic and the other to extrahepatic causes. The intrahepatic group comprised cases following infectious hepatitis and those caused by cirrhosis of the liver of other ætiology, whilst the extrahepatic group were due to congenital or acquired anomalies of that part of the portal system outside the liver. In pædiatric practice the latter group provided most of the cases referred to the surgeon, and it should be emphasized that the liver was macroscopically and microscopically normal in that group. In discussing investigations, Dr. Howard said that the first object in any case was to place it correctly with reference to the two groups. The initial step was the radiographic delineation of the portal vein and its tributaries, by what was generally called a portal venogram. This was most readily accomplished by injection of the spleen with contrast medium and subsequent X-ray examination of the portal area. The picture then produced could be termed a splenic portagram and provided critical information about the state of the portal vein itself. Should the portal vein appear normal, the block was in the liver and the case fell into the intrahepatic category. If the portal vein as such appeared absent or grossly distorted, the cause of the hypertension should be sought outside the liver, and the portagram would delineate the situation and size of the portal venous radicles, thus indicating the possibilities of effecting an anastomosis with a systemic vein. The actual œsophageal varices were usually well outlined. The portal venous pressure would be estimated whilst the needle was in the spleen. It was usually in the region of 400 millimetres of water. The upper level of normality of this pressure was a matter of some dispute, but it was probably 150 millimetres of water. An index of the portal venous pressure could also be obtained by catheterization of a radicle of the hepatic vein. The pressure elevation would, of course, be less pronounced than in an element of the portal vein. Should a patient already have been subjected to splenectomy, laparotomy would be necessary to obtain a portal venogram. A tributary of the superior mesenteric vein was injected and X-ray films were taken while the patient was on the operating table. The resulting picture was referred to as a mesenteric portagram. A piece of liver could be removed for biopsy at the same time. Operation should probably not be undertaken solely for the purpose of liver biopsy or even with the additional object of estimation of the portal pressure. In most cases the decision to operate could be made without examination of a section of the liver, and the portal pressure could be confirmed at the curative operation.

Dr. Howard said that liver function tests had not proved of value in the investigation. Severe and extensive liver damage had to be present to produce significant variations from normal. Œsophageal varices could be demonstrated with the aid of contrast X-ray pictures or be seen through the œsophagoscope, but these measures were not often necessary.

In regard to treatment, Dr. Howard said that if it should be established that a normal portal vein was present, a porta-caval shunt should be effected by end-to-side anastomosis of the portal vein with the inferior *vena cava*. This operation, when a right thoraco-abdominal approach was used, was not difficult and was well tolerated by the patient. More commonly, however, he said it would be found that the portal vein as such was absent or grossly abnormal. The treatment of election in such a type was probably some form of porta-caval shunt if this was feasible. The portal venogram would give valuable information on that point, but it was important to realize that large channels which were visible in X-ray films might not be located at operation, and further that operation might reveal vessels which were not visible in the films, but which were adequate for purposes of anastomosis. Dr. Howard stated that his own feeling was that the portal fissure should always be explored in the hope that a satisfactory porta-caval shunt could be effected. It should be remembered, he added, that the chance of such a vascular shunt remaining patent depended not only on the pressure differential between the two venous systems, but also on the size of the opening and the amount of blood it had to transmit. This made one doubtful of the advisability of employing anastomoses which involved the use of smaller veins—especially, of course, in children. Such an anastomosis was the spleno-renal, in which the veins concerned were apt to be small and which, if splenectomy was performed as part of the procedure, would probably not transmit a great deal of blood at the critical early period of its existence.

Dr. Howard stated that should no anastomosis be practicable, the next best procedure was probably a direct attack on the bleeding site. This could be effected by ablation of the extrinsic vessels of the upper two-thirds of the stomach and the lower third of the œsophagus augmented by transection of the stomach in its upper third, ligation of œsophageal venous columns and then resuture of the stomach. Splenectomy, he said, was indicated only when there was a localized block in the splenic vein. For that very rare type of case it was the perfect answer. In other cases it sacrificed valuable collaterals for merely a temporary benefit. Various methods of increasing collateral circulation had been advocated, but up to the present they had not met with reasonable success.

Dr. Howard said that there had been advocates of ligation of various branches of the cœliac axis. Splenic artery ligation undoubtedly had a place, either alone or in combination with other procedures. It reduced the amount of blood reaching the portal system without disturbing the collateral circulation at the back of the spleen and would also correct any secondary hypersplenism which might have developed. More extensive ligations, he said, had not fulfilled the hopes of their protagonists.

In discussing the treatment of the acute bleeding which did not yield to conservative measures, Dr. Howard stated that it was vital to realize that operation might succeed when conservative means had failed, and equally vital to pick the correct time for operative intervention. It would seem that the most obvious measure was a direct attack on the bleeding point by exposure of the upper third of the stomach and lower third of the œsophagus. Incision of the anterior surface of the stomach about an inch below the œsophageal junction gave an excellent view of the bleeding area. Measures to lower the portal pressure were probably better deferred until the state of emergency was past. The problem of whether and when to intervene in an actively bleeding phase was not unlike that of the bleeding peptic ulcer, and it was equally important in both conditions not to allow the patient's state to deteriorate to such an extent as to jeopardize his chances of recovery.

In conclusion, Dr. Howard said that it should be emphasized that all results should be interpreted in the light of the natural history of the disease which was characterized, in many instances, by spontaneous remissions which might last for years. This fact, combined with the relatively small number of patients presenting for treatment, made the evaluation of results extremely difficult.

Radiological Aspects of Portal Hypertension.

H. G. HILLER (Melbourne) discussed the radiological aspects of portal hypertension. He said that until recently the only radiological investigation for portal hypertension was an assessment of possible varices in the lower part of the œsophagus or in the stomach by means of a barium "swallow". The usefulness of this procedure was limited, as the presence of varices was often already suspected by previous bleeding, and their presence could not always be shown by barium. Dr. Hiller went on to say that contrast venography of the portal venous system had, however, greatly increased the scope of the radiologist, and that investigation had been gaining in popularity. The injection of contrast medium was usually undertaken percutaneously into the spleen, but if as sometimes happened splenectomy had already been performed, the same result could be obtained by injection into a tributary of the portal vein at laparotomy.

At the Royal Children's Hospital, Melbourne, Dr. Hiller stated, the preparation of a number of splenic portagrams had been undertaken. The routine procedure was that under general anæsthesia combined with a respiratory depressant such as "Scoline", a wide bore, short bevel needle was inserted into the spleen. Sometimes it was possible to feel the needle passing through the splenic capsule, but on other occasions the first intimation that the spleen had been punctured was the passage of blood from the needle. The portal pressure was then immediately recorded by an electromanometer, and then fifteen to twenty millilitres of 70% "Urokon" were injected by hand. Pressure equipment was never used for the injection because of the risk of rupturing the spleen. A series of films was then exposed at intervals of one second, the series starting one second after the beginning of the injection. On completion of the injection the needle was at once removed. Care was taken during the whole procedure to inhibit diaphragmatic movement by means of the respiratory depressant.

Dr. Hiller said that the radiological picture in the cases presenting at the Children's Hospital had been that of cirrhosis or of cavernous malformation of the portal vein. No cases of portal vein block had so far been demonstrated. Dr. Hiller showed examples, firstly, of the normal portal vein pattern. The pattern of cirrhosis demonstrated the venous branching in the liver which could hardly be distinguished from normal. The dilated varicose gastric and œsophageal veins were well shown. The pattern of the cavernous malformation was then shown. Here the venous distribution in the liver appeared abnormal and the venous branching was unlike that seen in the normal or cirrhotic patient. Dr. Hiller stated that biopsy studies in such cases had failed to show any pathological changes in the portal tracts. Again the varicose vessels were clearly visible.

In the interpretation of films, Dr. Hiller stated, two important points had to be remembered. The first was that on injection the dye followed the course of least resistance, and if wide anastomotic channels were present the main portal vein might not be filled. That should not be taken as evidence of a portal block. The second point to remember was that the veins could be grossly dilated and simulate the splenic or even the portal vein. Dr. Hiller demonstrated these points in a series of X-ray films.

In conclusion, Dr. Hiller said that it would appear that the method was a safe procedure which was very useful in diagnosis and in the planning of surgical treatment for portal hypertension. It could often be used post-operatively to show the presence of a patent porta-caval or other shunt.

F. DOUGLAS STEPHENS (Melbourne) opened the discussion. He said that while the methods of diagnosis of portal hypertension in childhood were very good, the treatment was most unsatisfactory, as in most cases the condition was due to a cavernous malformation of the portal vein. Thus there was scope for experimentation. After experimentation on dogs, Dr. Stephens had applied the following technique to a child. A portion of transverse colon with its intact blood supply was mobilized and buried beneath the skin of the lower part of the chest. It was then incised longitudinally and stitched down to the chest wall. The edges of bowel were sutured to the skin in an attempt to produce a collateral connexion between portal and systemic venous channels. The surface of bowel was then covered by split skin grafts after mucosa had been stripped off. This showed, after sixteen months, a red blush of non-pulsatile blood vessels at the mucosal-skin margin, with small collecting veins radiating towards the axilla. The portal pressure prior to this procedure was 400 millimetres of water. At the original operation the splenic artery was ligated. Post-operatively, the pressure in the skin veins was 110 millimetres of water. Though the pressure in the skin veins was now higher than normal systemic venous pressure, that represented a reduction of the original portal venous pressure. Anastomoses had taken place. Time alone would show the ultimate result.

Dr. Stephens stated that in cases in which the splenic artery and vein had been ligated the spleen should be left *in situ* so that a post-operative portal venogram could be taken. This enabled the surgeon to tell if his anastomotic operation had been satisfactory. In one case this technique had enabled him to demonstrate occlusion of a previous anastomosis. By leaving the spleen there was also no interference with any collaterals which were frequently found around the splenic hilum and capsule.

D. COHEN (Sydney) stated that he had fully discussed with Milnes-Walker and Alan Hunt, of Saint Bartholomew's Hospital, the problem of portal hypertension in childhood. He felt that once a diagnosis of portal hypertension was established, the following routine was most satisfactory—œsophagoscopy, the preparation of a portal venogram, liver biopsy and measurement of portal pressures. These procedures should be undertaken at the one sitting, and should then enable the surgeon to proceed with definitive surgery. He said that he regarded portal venography as a dangerous procedure unless carried out under strict control with general anæsthesia and relaxant drugs, and quoted three cases in which peritoneal hæmorrhage occurred after splenography. He regarded a porta-caval shunt as the only satisfactory shunting procedure. Milnes-Walker had had no further bleeding in children with portal hypertension when this procedure only was used. He agreed with Dr. Howard that a satisfactory liver biopsy was obtainable only at laparotomy. In regard to portal pressures, Dr. Cohen felt that only open procedures were satisfactory.

T. Y. NELSON (Sydney) asked Dr. Howard how he demonstrated the site of bleeding in the cases under discussion.

In reply to Dr. Nelson, Dr. Howard stated that the only satisfactory method was to open the upper third of the stomach and inspect the area. That also allowed good vision of the lower one to one and a half inches of the œsophagus. In this way the bleeding point was seen and could be readily ligated. Dr. Howard further stated that the upper third of the stomach was the commonest site of bleeding in those cases. He had applied the technique described satisfactorily in the past in two cases.

The Syndrome of the Pseudotruncus Arteriosus.

MOSTYN POWELL (Melbourne) presented a study of fifteen cases of *pseudotruncus arteriosus* occurring in a series of approximately one thousand patients with congenital heart conditions seen at the Royal Children's Hospital, Melbourne. In discussing the symptomatology and clinical features, Dr. Powell said that the symptoms were relatively mild; as infants the patients throve quite well, as children they had moderate dyspnœa but quite fair exercise tolerance, and in one case at least adult life had been reached and maintained in fair comfort. Cyanosis was mild and at times barely noticeable. Examination of the heart showed little of specific nature, the precordium was notably free from bruits in most cases, but well out in the lung fields, usually maximal in one or other axilla, and a well-marked continuous bruit was audible. This bruit was not in the ductus area and combined with the cyanosis formed a striking diagnostic feature of the *pseudotruncus arteriosus*. The blood pressures were normal. The electrocardiogram showed a right-sided graph with a right ventricular hypertrophy pattern. Usually polycythæmia and high hæmoglobin values of the right to left shunts were present. Radiographic and angiographic findings were classical. Dr. Powell said that in his series cardiac catheterization had been unsuccessfully attempted in one case only, and it appeared unnecessary as a diagnostic weapon in this type of lesion. The only points in differential diagnosis were between an arterio-venous aneurysm of the lung which was eliminated by radiographic findings, or a tetralogy of Fallot with an open *ductus arteriosus*, in which the continuous murmur was in the ductus area and radiological features were different.

In discussing the pathological anatomy, Dr. Powell said that the basic abnormality was pulmonary artery atresia,

due, it was thought, to grossly unequal division of the primitive *bulbus cordis* by the aorto-pulmonary septum. This atresia did not necessarily extend throughout the two main branches of the pulmonary artery, but certainly was present at its origin, thus precluding its junction with the right ventricle. Under these conditions two other possible channels remained for blood supply to the lung fields, namely, the bronchial arteries and the *ductus arteriosus*. In this lesion it was the bronchial arteries which enlarged to massive proportions, entered into communications with the pulmonary system near the hilum of the lung and thereby produced the arterio-venous shunts and curiously placed continuous murmurs which were the hall-mark of the condition. Sometimes other vessels entered the picture, as in a case of Allanby *et alii*, in which an abnormal artery left the aortic sinus close to the left coronary artery and entered the pulmonary artery above the atresic valves. Dr. Powell said that the bronchial arteries, normally three in number, arose from the upper part of the descending aorta; occasionally one arose from the first or second intercostal artery. They supplied the bronchi and extended as far as the alveolar ducts, the return being mainly via the pulmonary veins. No large anastomoses occurred with the pulmonary system except under exceptional circumstances such as the condition under discussion. The aorta which was the sole outflow tract from the heart was huge and overrode the interventricular septum. No pulmonary arteries arose from the aorta, as in the true *truncus arteriosus*, a lesion of great rarity in which the primitive aorto-pulmonary septum had never appeared. The aorta had been right-sided in a high proportion of the cases.

Dr. Powell went on to say that the role of the *ductus arteriosus* in this lesion was of interest. It was suggested that the reason the bronchial arteries were so large and freely communicable with the pulmonary arterial system, even at birth, was that, in addition to pulmonary atresia, there was also an atresic non-functioning *ductus arteriosus* throughout intrauterine life. As could be seen from the cat embryo models of Huntingdon, this delegated to the bronchial arteries the sole blood supply to the developing lungs. The intimate relations of the pulmonary and bronchial supply in the primitive pulmonary plexus explained the ready establishment of the large shunts so characteristic of the condition. In the tetralogy of Fallot such shunts would be advantageous, but the presence of a normal *ductus arteriosus* prevented this development, and in the presence of the tetralogy it was not for some years after birth that the bronchial arteries enlarged appreciably. Dr. Powell said that this theory was not easy to prove, for it was difficult to say whether a *ligamentum arteriosum* had ever been a functioning *ductus arteriosus*. A series of cases reported by Allanby *et alii* certainly did not disprove it. In fact in one post-mortem examination a very large bronchial-pulmonary artery shunt was reported in which the ductus was not mentioned at all and no sign of a ligament could be seen in the illustration of the lesion.

In discussing treatment, Dr. Powell said that it was usually conservative as most patients were relatively well. If deterioration occurred it could be possible to increase the flow to the lungs by a Blalock anastomosis. If so, the anastomosis should be made on the side opposite to the loudest continuous murmur, for that was the side receiving maximum bronchial flow; however, collapse of that lung for operative purposes could be fatal, as had been shown by Roche.

In conclusion, Dr. Powell said that this was a readily diagnosed cyanotic congenital heart lesion, termed the *pseudotruncus arteriosus*, which in most instances had a comparatively benign course, had a diagnostic combination of signs in the form of cyanosis accompanied by a continuous murmur in the lung fields remote from the ductus area, and had characteristic radiographic findings. It differed from the true *truncus arteriosus* in that the pulmonary artery, though atresic, had been differentiated by the aorto-pulmonary anastomoses. Treatment was conservative as a rule because of the relative well-being of the patients.

Radiological Appearances of the Pseudotruncus Arteriosus.

H. G. Hiller (Melbourne) presented the radiological features of the *pseudotruncus arteriosus*, and showed a series of films demonstrating the salient radiographic and angiographic findings. He said that the radiological picture of pseudotruncus was unique. The outstanding features on an X-ray film were, first, the nodular congestive changes in the lung fields; these were often more marked in the upper zones and in no way resembled the anatomical architecture of the pulmonary arterial tree; the changes were due to the enormously enlarged bronchial arteries. Secondly, the markedly tip-tilted cardiac apex was associated with other radiological evidence of an enlarged right ventricle. Thirdly, a very high percentage of right aortic arch occurred in 70% of cases. Other important findings were the absence of a normal pulmonary artery shadow in the antero-posterior view and the frequent appearance of œsophageal indentations by the bronchial arteries on a barium "swallow".

Dr. Hiller said that in eleven of the cases at the Royal Children's Hospital angiocardiographic studies had been made, and in all a typical appearance had been demonstrated. The huge outflow tract overlying both ventricles had filled at once from the right ventricle and in most cases the bronchial arteries could be seen arising from it. Often an insignificant right ventricular outflow tract, dwindling away to nothing, was seen, especially in the right anterior oblique position.

D. Stuckey (Sydney), in opening the discussion, said that pulmonary atresia was not uncommon in the older child (three to four years of age group) who presented with cyanosis, clear lung fields, marked disability and a murmur in the precordial region. The murmur could be continuous and could occur in an unusual site. He said that the cases described by Dr. Powell differed in that cyanosis was not marked, disability was not so great and the children were in a younger age group. Another condition which could cause confusion was the true truncus with one large arterial trunk. In such cases the blood supply to the lungs was by large blood vessels arising directly from the trunk. In those cases a continuous murmur did not occur. In the type of case described by Dr. Powell it was very difficult to decide whether a small pulmonary trunk was actually present even at autopsy, and he asked Dr. Powell if he had any autopsy evidence to confirm aplasia of the pulmonary conus.

D. Cohen (Sydney) had seen two patients with this condition at operation. They differed from Fallot's tetralogy and were not cases of true truncus, although they did have a single outflow tract. Bronchial vessels arising from the aorta were enormous. Operative treatment of the condition was not indicated as a Blalock operation could not improve the blood supply to the lungs. Dr. Cohen would regard a continuous murmur as a direct contraindication to operation.

Dr. Mostyn Powell said that he had no autopsy evidence to show atresia of the pulmonary conus, but considered that angiocardiographic studies were conclusive. He agreed that operation was not indicated, although it had been attempted in some cases described in the literature. At birth the children virtually had three "Blalock operations" already, and adding another, even if this was possible, was not going to improve the blood supply to the lungs to any great extent. He said that most of these children were relatively well and frequently cyanosis was not obvious.

Renal Tubular Disease.

N. Chalk (Brisbane) read a paper entitled "Renal Tubular Disease". He said that by definition renal tubular disease signified failure on the part of the renal tubules to discharge adequately one or more of their regulating functions, while at the same time there was no evidence of altered glomerular function. Clearly in a progressive renal lesion it would be expected that a tubular glomerular defect would be revealed first, and that other defects would appear with the passage of time; thus what might pass as a tubular defect today might become in one to two years an all too obvious total renal insufficiency. Therefore, reservations had to be made before these children were presented; no balance techniques were available, no measurement of glomerular filtration rate was performed with inulin, and, most important, there was no long follow-up period. Dr. Chalk said that renal acidosis was the best known example of the disease, and it sufficed to say that infants suffering from it presented as failures to thrive occasioned by vomiting and anorexia, and the characteristic feature was their acidosis while they were secreting a urine which was alkaline or nearly so. They showed no rise in non-protein nitrogen, except when severe vomiting occasioned prerenal ozotæmia. Vomiting might result in a deviation from the usual hyperchloræmic acidosis. In this disease there was a failure of reabsorption of bicarbonate with some attendant loss of fixed base, and the excessive excretion of bicarbonate inhibited to some extent the ammonia production by the tubules—so much so that for some time it was considered that this was the primary lesion. Subsequently investigations showed that ammonia production in this disease was quite normal. Renal tubular disease might also manifest itself as a failure to conserve base, and failure to reabsorb aminoacids, water and perhaps calcium.

The first of the children Dr. Chalk discussed had come under observation eighteen months previously, and at that time she was nineteen months old. Her mother had had a normal pregnancy and labour and this child had thriven up to the age of nine months, when her weight curve flattened out and she lost her appetite. Nothing further was noted and she did not vomit. For the next seven months she was regarded as presenting a teething problem, but her teeth failed to appear, and towards the end of that period her personality changed—she became irritable, frustrated both parents and relatives and refused to do anything other than sit or lie. At nine months she was standing in her cot; at eighteen months she could only sit, and then with considerable kyphosis. It was small wonder, therefore, that she was at last diagnosed as suffering from pink disease. Examination at this time showed gross hypotonia, but she had none of the other characteristics of acrodynia: no sweating, no rash, no hypertension, and no increased urinary excretion of mercury. She showed slight vasomotor changes in her extremities. Her hair was sparse, coarse in texture and short in length—the last being the result of its brittleness. She had had no hair cut for three months when first seen, and it was this single feature which had caused her mother most concern. She was a wasted child with a pot belly, the skin hung in a fold over her buttocks, and she had thin thighs through which the femora could readily be palpated. Muscle wasting had resulted in a rectal prolapse. Her appearance and temperament had caused her to be labelled "a cœliac" for a time, but there was no response to dietary treatment and she had none of the stigmata of steatorrhœa. Her mental activity was in accord with a wasting disease—she sat still, neither crying nor smiling, entirely disinterested in her surroundings. Her face showed the least wasting. Apart from the above, she showed a moderate hypochromic anæmia, presumably the nutritional result of her anorexia. The results of all routine clinical and chemical tests proved normal. This child, when given a dose of calcium chloride on the basis of 100 millimols a day, showed virtually no increase in her output of ammonia on the third day, although the output of sodium, potassium and calcium increased considerably. The figures shown revealed no information except that, when acidotic, the child's excretion of ammonia did not increase. Later this technique was abandoned and Talbot's recommendation of ammonium chloride in a dose of six grammes given twice in twenty-four hours was followed. Interestingly, her ammonia production was halved after administration of "Diamox" and not increased by infusion of phosphate. Only an insignificant increase accompanied a water diuresis and was depressed during solute diuresis. Dr. Chalk said that these findings gave a lead in explaining the physical findings. The length of history obviously implied that the tubular defect was of long duration. The fact that she was a normal infant from birth to nine months was most likely due to the fact that her tubules were able to cope with the total load of fixed acid requiring excretion, until such time as her surface area put greater demands on her kidney function. When this occurred the fixed acids could be excreted only with fixed base—sodium, potassium and calcium. There resulted then a loss of fixed base to the body; hence the loss of weight, the poor growth of hair, the loss of muscle tissue, resulting in hypotonia, pot belly and wasted buttocks; and the severe osteomalacia of the second child was mitigated in the first by her milk diet.

The second child had been referred with a diagnosis of pseudohypertrophic muscular dystrophy, because he climbed his legs when standing. His urinary ammonium excretion was never more than 40 milliequivalents per litre, and he presented the same features, but his hair loss was less noticeable and his mental change less severe. Difficulty was experienced in the attempt to increase his urinary ammonium output because he became so rapidly acidotic and vomited most of his acidifying load. However, he showed marked osteomalacia which took more than nine months to clear. With treatment he showed similar progress to the other child. In treatment Dr. Chalk said that fixed base had to be supplied along with anions which could be metabolized. The customary therapy of renal acidosis was sodium citrate and citric acid; but the prolonged administration of sodium salts resulted in an excessive excretion of potassium, and for this reason a mixture of sodium and potassium citrate was given, alkalosis being watched for on the one hand and signs of potassium toxicity on the other.

Dr. Chalk concluded by saying that he presented this as a preliminary report on two children. The suggestion was made that careful administration of ammonium chloride might unmask renal tubular insufficiency in infants whose failure to thrive was a cause for concern. Several problems were unanswered—among them the greater wasting in one child able to manufacture more ammonia, and the depression of ammonia production by "Diamox". It was pointed out that ammonium chloride had caused clinical acidosis and dehydration in two instances, and in one of them, while no glomerular disease was apparent, administration of base had not corrected the failure to thrive.

JOHN PERRY (Melbourne), in opening the discussion, stated that Dr. Chalk's first case was explained very well on a physiological basis. He stated that the body produced the equivalent of one to two litres of concentrated hydrochloric acid per day and an equivalent amount of base to neutralize this. Actually this was not quite so, as there was a deficiency of between 50 and 100 milliequivalents of base. In Dr. Chalk's case, acid production was normal, but because of deficient ammonia production by the kidney there was insufficient base for its neutralization. Sodium, potassium and calcium were consequently used in place of the ammonia. This resulted in a total depletion of these ions.

Dr. Perry said that he could not help in regard to the ætiology of the condition, but he felt that the significant factors were firstly that the passage of time might produce results showing the condition to be a specific renal tubular defect. There was in the case no evidence of a glomerular defect. Secondly, the child might later show evidence of further renal tubular dysfunction with amino aciduria, cystine deposits in bone marrow or optic lens, hypokalæmia and rickets. Dr. Perry concluded by congratulating Dr. Chalk on a most physiological approach to the problem and sympathized with him in his difficulties in obtaining satisfactory biochemical assistance.

Pneumocystis Pneumonia.

R. D. K. REYE (Sydney) presented two cases to demonstrate a variety of parasitic pneumonia which, though occurring commonly on the continent of Europe, had not been described before in Australia. Salient features of the clinical histories and the pulmonary pathology of the two patients were described and a brief résumé was given of the more important features of the disease as obtained from a study of the literature.

His first case was that of a girl who had been ill for twelve months and who had suffered from increasing dyspnœa and cyanosis with an unproductive cough over that period. Fever had not been a feature of the illness at any time. The pathological changes in the lungs proved most unusual. To gross inspection the lungs were uniformly solid and airless, and on microscopic examination the entire air-containing tissue of the lung was filled with an amorphous granular material which did not resemble any variety of inflammatory exudate. The second case which, in fact, had occurred several years earlier and was found by a retrospective survey, was a much more typical example of the disease and provided material in which the parasites, the *Pneumocystis carinii*, could be recognized without difficulty. The second patient was a female infant who had been treated for recurrent staphylococcal infections since the age of four days. She failed to thrive, and by the age of six months was known to be suffering from a pneumonic process which did not respond to treatment and from which she died one month later. The pulmonary pathological change was quite typical in this case. Microscopic examination of the lungs showed very clearly the broad alveolar septa packed with lymphocytes and plasma cells and the honeycomb-like material in the alveoli produced by the mucoid capsules of countless parasites. Dr. Reye pointed out that, because of the unusually long illness in the first patient, the pathological changes in the lungs varied from those usually found; but that as a result of experience gained from a study of the second case it was possible to find a small number of viable parasites in the first case and so to establish a firm diagnosis.

Dr. Reye went on to say that the parasitic nature of the disease had been recognized only as recently as 1952, and though the exact nature of the parasites was not entirely agreed upon, the majority of those with experience of the disease held the opinion that the parasites were protozoa. The disease, under the name of interstitial plasma cell pneumonia, had been known on the continent of Europe for a long time where it occurred sporadically or in the form of small epidemics in nurseries. Only very few cases had been described as occurring in other countries.

Dr. Reye said that with very few exceptions the disease was one of infants under the age of six months; premature and poorly nourished infants were especially susceptible. The onset was insidious; the infants became languid, with

anorexia and a gradual increase in respiratory frequency, but there was no fever. Within two weeks of the onset, dyspnœa and cyanosis were pronounced. The mortality rate was high, reaching 40% in some series, but if the patient survived, recovery was to be expected in four to six weeks.

Dr. Reye expressed his indebtedness to Dr. R. E. J. ten Seldam, who had first suggested that the first case might possibly be an example of pneumocystis pneumonia; his help with the study of the foreign literature was invaluable.

Alan Williams (Melbourne) asked Dr. Reye if the children were New Australians. He stated that he had been looking for such a case in Melbourne, but so far had not seen the condition. In Europe the diagnosis was frequently made during life. Now that Dr. Reye had shown that the disease occurred in Australia, Dr. Williams said that it should be considered in differential diagnosis. Dr. Reye's first patient had presented at an unusual age. The patients usually first appeared in the nurseries and premature wards and were infants up to the age of four months.

Stanley Williams (Melbourne) stated that in the army he had once been confronted with a trypanosomiasis-like organism, which was subsequently found to be due to contamination of staining materials. He certainly did not wish to imply that this was so in Dr. Reye's case. He asked Dr. Reye if this protozoan was prevalent in Australia.

D. Jackson (Brisbane) had observed in dogs a similar clinical and pathological picture to the one Dr. Reye had described. He had wondered if the illness he had witnessed, and which did not respond to treatment, was *Pneumocystis carinii*.

In reply to Dr. Alan Williams, Dr. Reye stated that he had interviewed the parents of the first patients. There were four siblings alive and well. The family was Australian and had had no contact with New Australians, and the parents had never been abroad. He said that he was unable to trace the family in the second case.

In reply to Dr. Jackson, Dr. Reye stated that although this protozoan could be found in animals, it did not produce symptoms. Symptoms might be found in suckling mice, but not in mature mice.

In reply to Dr. Stanley Williams, Dr. Reye did not think that contamination of staining material had occurred. Dr. Reye further stated that the parasite was demonstrable only with certain stains. He went on to say that an association of this condition had been found with cytomegalic inclusion disease. Approximately a quarter of the cases on the Continent had had this association. In Baar's case reported in England this association had also occurred.

In conclusion, Dr. Reye said that it appeared that such conditions as agammaglobulinæmia and cytomegalic inclusion disease predisposed to *Pneumocystis carinii*. Cytomegalic inclusion disease had recently been described in adults, and in some of the cases an interstitial plasma cell reaction in the lungs had been demonstrated. Cytomegalic inclusion disease did not produce this change which was now felt to be due to *Pneumocystis carinii*.

The Treatment of Congenital Dislocation of the Hip by the Denis Browne Method.

Peter Jones (Melbourne) reported the short-term results in twenty consecutive new cases of congenital dislocation of the hip treated at the Royal Children's Hospital, Melbourne, between 1950 and 1956, by the Denis Browne method. In discussing the reduction of the dislocation, he said that the method commenced with manipulation under general anæsthesia, the child lying prone on a low table. Reduction was effected by pressure on the greater trochanter of the femur with one hand, while the other flexed the affected hip and circumducted the knee through a small circle of movement. The femoral head was thus made to retrace the course taken during dislocation and entered the acetabulum over the posterior rim, under the effect of trochanteric pressure directed along, not across, the neck of the femur. Dr. Jones said that reduction was then maintained by abducting the affected hip into the traditional "90°, 90°, 0°" position, 90° flexion, 90° abduction and 0° rotation. This position provided stability for the femoral head in its new reduced position by utilizing the only two strong anatomical structures present. These were the ilio-psoas tendon passing tangentially across the anterior surface of the hip joint capsule, and the ilio-femoral ligament. In the position described this Y-shaped tendon was disposed so that the limbs of the Y were in contact with the femoral head superiorly and posteriorly. A plaster of Paris cast was then applied over adhesive felt strips (which covered the posterior superior iliac spines) and flannelette bandage which was coextensive with the plaster, reaching from umbilicus to the ankle of the affected side and to the knee of the other side if unaffected. During application the prone position was maintained by pressure on the sacrum, the lower half of the patient being suspended free of the table by a supporting hand beneath each knee. No special rest, frame or table was required. Radiological confirmation of reduction was obtained, and after one month the plaster was replaced by the Denis Browne splint.

Dr. Jones said that the splint consisted of two half-circle metal cuffs completed and covered with soft chamois leather, forming two circlets, one of which enclosed the distal third of each thigh. These circlets were joined by a metal bar which passed along the posterior aspect of the thighs. The bar was capable of elongation to accommodate longitudinal growth in the femora and was held in place by a fabric loop attached to a webbing waist band. Active movements were encouraged as soon as the splint was applied; locomotion was soon possible, crawling, scuttling or even walking, depending on the patient's age. He said that the splint was unique in that it maintained full abduction at all times, yet allowed a wide range of movement, especially rotation at the hip joint around the longitudinal axis of the femur. When acetabular growth had progressed sufficiently (assessed radiologically), usually after six to ten months, the splint was discarded. No other position was contrived, and a transition phase ensued during which adduction and full hip movements were regained. Dr. Jones then showed a short motion picture demonstrating the method of reduction, application of plaster and the range of movement and ambulation of children wearing the Denis Browne splint.

Dr. Jones said that the series consisted of twenty consecutive unselected cases of congenital dislocation of the hip, eleven of which were bilateral—making a total of thirty-one hips. The age at which diagnosis was made varied from one month to four years nine months. The average age was eighteen months. The twenty cases were comparable with other large series as regards sex, family history and associated anomalies. He said that the results reported were short-term results only, and evaluation of the method at that stage rested upon the proportion of "stable reduced" hips. The criteria for that accolade were firstly clinical as shown by the absence of the characteristic rolling gait of a dislocated hip and a negative response to the Trendelenburg test, and secondly radiological, as shown by a femoral head adequately contained in a suitably shaped acetabular fossa. Of the twenty cases, eighteen only could be reported on as splints were still being used in two. All eighteen cases showed stable reduced hips as previously defined. This compared favourably with Putti and Scagliatti's 94% satisfactory results in 119 treated patients under one year old, and Muller and Seddon's 73% among 292 patients treated *ab initio* at the Royal National Orthopædic Hospital.

Dr. Jones went on to say that though the stability rate was gratifying, certain qualifications had to be made in a small number of cases. One patient had a limp, but gave a negative response to the Trendelenburg test, recovering osteochondritis being the cause. Two patients had a limited range of movement, each in one hip. Both these patients had bilateral dislocations, and the relevant hip in each instance was the site of osteochondritis. Both patients required prolonged periods of splinting, for redislocation occurred in one hip after the initial splinting. One of these patients was the oldest child in the series (four years nine months at the commencement of treatment). In both cases the range of movement was steadily improving and they conformed to the other criteria.

In discussing the radiological results, Dr. Jones said that 20 hips (of the total 31) were unaffected by osteochondritis, and the femoral head in each of these was normal in outline, size and shape, except one which showed minimal flattening. In the remaining eleven hips "osteochondritis" occurred and only two were radiographically normal. The remaining nine showed varying degrees of flattening or some irregularity of outline. "Osteochondritis" was thus responsible for the relatively unsatisfactory radiological results in this series. The incidence in other reported series varied from 30% to 45%, mentioned by Trueta, to 51% in Severin's series of patients treated after the age of two years. The exact pathological process underlying the cycle of radiological changes was unknown, and the relationship it bore to Legge-Perthes's disease remained conjectural. It had been suggested that in congenital dislocation of the hip there might be interference with the vascular supply to the epiphysis of the femoral head during or after reduction. The vessels, branches of the *circulus vasculosus* of William Hunter, reached the epiphysis along the posterior aspect of

the capsule of the hip joint and to a lesser extent via the *ligamentum teres*. It was the aim, in the future treatment of congenital dislocation of the hip, to reduce the incidence of osteochondritis, and there appeared to be two means of doing this. Firstly, earlier diagnosis was essential. Analysis of the incidence in the present series showed that in those cases in which treatment was commenced before the age of fifteen months the incidence of osteochondritis was half of that noted when treatment was commenced after the age of fifteen months. Secondly, in a new series of cases, reduction was being effected by a traction divarication method. Once reduction had been achieved the patients would be treated by plaster immobilization for one month and then by the Denis Browne splint, as described. The results of this series would be the basis of a subsequent report.

Finally, Dr. Jones said that certain conclusions had been drawn from experience of the use of the Denis Browne method. These were, firstly, that reduction could be achieved by manipulation without special apparatus. Secondly, the splint which was the keystone of the method permitted active movements in the coronal plane, which stimulated development of the hip joint musculature. These movements also stimulated acetabular development. Thirdly, the wide nursing area, the convenience of the splint and the ambulation it allowed permitted the easy management of these children by the mother at home after initial reduction of the dislocation in hospital. The period of splinting could be prolonged as long as necessary should acetabular development be slow. Lastly, anteversion and interposition of soft tissues between femoral head and acetabular fossa had presented no problems in Dr. Jones's series, though they might have done so if the series had comprised older children. Arthrography had been used in only one case, and had not been an integral part of the regime.

In conclusion, Dr. Jones said that he would like to express his gratiudte to Dr. Douglas Stephens for access to the patients and to Dr. Denis Browne for his instruction in his method of treatment.

DOUGLAS MCKAY (Adelaide), in opening the discussion, expressed the opinion that Denis Browne's method had great merit and considered that his early diagnosis and treatment of congenital dislocation of the hip were outstanding contributions to pædiatric surgery. Dr. McKay said that whereas in Australia the treatment of congenital dislocation of the hip was very sound, this was not always so on the Continent where operation appeared to be frequently necessary through failure of more conservative measures. Dr. McKay next commented on Denis Browne's ability to make the diagnosis early, even at times before the radiologist was prepared to admit the dislocation. On clinical examination of a suspected subject he flexed the thighs to a right angle and found considerable limitation of abduction from this position on the involved side. The confirmatory X-ray examination might merely show the position of the femoral head, if present, to be a little lateral and a little high. Dr. McKay next mentioned that Denis Browne now used his bar in the posterior position with a "Sorbo" rubber pad to protect the sacrum. With this form of treatment both the mother and the child were extremely happy and cooperative.

K. B. FRASER (Brisbane) regretted that the film had not shown the ability of the patients to walk in the squatting position without the use of the hands. He said that he had watched these children do this with great interest and amusement; they resembled Cossack dancers and had almost equal agility. Another position which older children sometimes learned to adopt in the Denis Browne splint was the capacity to stand on one leg. With the pelvis tilted, as it had to be, the abduction was not reduced as much as it appeared to be and, as Browne pointed out, the strong contraction of the *gluteus maximus* in that position prevented any posterior displacement of the head of the femur. Another important point, Dr. Fraser said, in this method of "treatment with function" was that the pelvi-trochanteric muscles, which were inevitably stretched while the dislocation was present, were given an opportunity to develop normally because of the hip joint movement allowed, and this in itself helped to hold the head of the femur firmly within the acetabulum. Finally, Dr. Fraser stated that it had to be remembered that in a minority of cases—three in a series of thirty treated by Dr. Lahz in Brisbane—such pronounced anteversion of the head and neck of the femur was present that it was necessary for treatment to be carried out in abduction, with internal rotation of the femur, and these cases were not suitable for treatment by the method described.

STANLEY WILLIAMS (Melbourne) asked if some plan of X-ray examination of all infants between the ages of three and six months might lead to earlier diagnosis.

J. STEIGRAD (Sydney) commented that the treatment of congenital dislocation of the hip in Sydney was almost completely in the hands of orthopædic rather than general surgeons, but he felt prompted to make several remarks. Firstly, he said that he had reviewed a series of cases of congenital dislocation of the hip twenty-five years previously and found a very high incidence of osteochondritis and redislocation. That resulted in an increased tendency to treat the condition by open operative reduction and shelf operations, and the trend appeared to be continuing. Secondly, he pointed out that in the 1920's Sir Robert Wade had tested small infants for what he called the "dislocable" hip by "abduction in flexion" as described by Dr. McKay, and finally that Dr. P. L. Hipsley regularly used a splint which, while made of wood, very closely resembled the Denis Browne splint.

Dr. Steigrad asked Dr. Jones if, when the splint was temporarily removed, it was necessary to maintain the position of abduction of the hips, and whether the special mobile chair was used for these children.

Dr. Jones, in reply to Dr. Stanley Williams, said that a clinical approach was more valuable in detecting the presence of congenital dislocation of the hip in the first three months of life in view of the inconclusive X-ray appearance at that age.

In reply to Dr. Steigrad, Dr. Jones stated that the splint was not removed at any time prior to its final removal after six to ten months. The chair, he stated, was not used because the children were either too young or were walking well already.

Eventration of the Diaphragm.

ERIC GOULSTON (Sydney) presented a résumé of eventration of the diaphragm and case histories of five infants, and of one adult with rupture, and a post-mortem specimen illustrating the condition. He said that the term was accepted as meaning marked elevation of all or part of one hemidiaphragm due to a congenital aberration in development. Its complex embryonic formation subjected this musculofascial structure to areas of potential weakness which were aggravated by the strain of a relative negative pressure in the thorax and the inspiratory muscular pull. Wrong timing, failure of adequate fusion and failures of development led to weak points, and there were therefore great opportunities for variation in size and shape as well as defects to occur. Congenital hypoplasia with non-development of muscular elements was accepted as the causation, and the involved diaphragm a mere fibrous sheet of atrophic membrane which contained few or no muscular fibres in its peripheral rim. The hemidiaphragm might function paradoxically if phrenic innervation was also faulty. The stomach angulated upwards, compressing the lung and displacing the heart and mediastinum, causing cardio-respiratory embarrassment. Eventration might be total, which was more frequent on the left, or partial, which was commoner on the right side, where the appearance might be mistaken for an accessory liver lobe. It was sometimes associated with *arthrogryposis congenita*. The incidence was said to be one in ten thousand.

The symptoms varied from none at all to varying degrees of dyspnœa and cyanosis and were referable to the cardio-vascular, respiratory or digestive system. Dr. Goulston said that the diagnosis was usually established by X-ray examination which revealed an abnormally high position of the affected hemidiaphragm with a smooth unbroken arc, and the heart and mediastinum displaced toward the normal side. As diaphragmatic movement was due to varying pressure in the thorax and abdomen as well as the muscle itself, normal motion might be seen, but usually fluoroscopy revealed lessened respiratory excursion and occasionally paradoxical movement.

Barium studies might help in differentiating the condition from a diaphragmatic hernia in which the diaphragm was more difficult to outline and pneumoperitoneal studies might be of value. Complications, while rare, did occur, and rupture of the thinned-out portion of the diaphragm during labour had been reported. Peptic ulceration, volvulus of the stomach, and pneumonia from inadequate pulmonary expansion might occur.

Treatment, he said, varied according to the severity of the symptoms and had to be as prompt in the newborn with cyanosis and dyspnœa, as when caused by diaphragmatic herniation. When indicated by cardio-vascular or

respiratory distress, surgical intervention by thoracic, abdominal or thoraco-abdominal approach was made. The diaphragm was repaired by plication or overlapping with interrupted non-absorbable sutures, tantalum or nylon mesh reinforcement being used if necessary. In tiny infants the abdominal approach was considered easier, while a thoracic approach gave better access in older children or adults. Dr. Goulston said that complete eventration had been repaired in the newborn by suturing the anterior portion of the diaphragm to the circumference of the costal margin of the diaphragm anteriorly, and the posterior portion to the crus medially and renal fascia laterally. The liver in such cases had no peritoneal attachment to the diaphragm and was easily mobilized. If after replacement it was found that the abdomen was too tense, only the abdominal skin wound was sutured as described by Gross for diaphragmatic hernia.

Dr. Goulston then presented the following case reports.

CASE I.—N.H., aged five days, had been sent to the Royal Alexandra Hospital for Children by Dr. Winning in 1951 with a history of grunting respirations and repeated cyanotic attacks. After admission the baby's condition remained good, there was no cyanosis or distress, and after three weeks' observation the baby was discharged. Chest X-ray examination showed the left hemidiaphragm markedly elevated, with the heart and mediastinum displaced to the right. The left dome moved evenly with the right. He had remained well since, having had a circumcision in 1952, and bronchopneumonia in 1953. A chest X-ray examination in 1955, when he was still symptom free, had shown marked elevation of the left hemidiaphragm with the heart and mediastinum still displaced to the right side.

CASE II.—K.B. had been admitted under the care of Dr. Vickery in 1954, aged three weeks, with a history of cyanosis, except when oxygen was administered, and rapid respirations. A Cæsarean operation had been performed at his birth on account of a shoulder presentation. After admission to hospital the baby appeared to be in no distress. A chest X-ray examination revealed an elevated right hemidiaphragm which moved paradoxically, suggesting phrenic paralysis. A barium study showed that the distal end of the stomach was much higher than the cardia owing to elevation of the liver. This baby was discharged after two weeks' stay in hospital and had remained symptom free since.

CASE III.—D.F., aged six years, had been admitted under Dr. Nelson's care in 1953 with a history of chronic cough and recurring attacks of vomiting since birth. A chest X-ray examination had shown the anterior two-thirds of the left hemidiaphragm to be elevated, and this portion exhibited paradoxical movement. The posterior third was normally attached and contracted normally with the right side. The heart was displaced to the right, and the stomach rotated anti-clockwise. Scoliosis convex to the left was present. Thoracotomy was performed and the redundant portion of the thin fibrous central portion of the diaphragm excised with suture of the muscular margins. Histologically the tissue examined consisted entirely of compact acellular bands of collagen and was devoid of any striated muscle. The subsequent history of the girl showed that she continued to vomit, especially after lying down at night, and a further chest X-ray examination revealed the similar original bulge of the left hemidiaphragm. Thoracotomy was repeated later and the defect closed by a *fascia lata* reinforcement. She had been well since.

CASE IV.—J.H., aged seven years, had been operated upon two years previously for repeated episodes of bronchitis, when a chest X-ray film showed a large eventration in the left hemidiaphragm. At thoracotomy the central membranous area of the diaphragm was excised, sutured at the margins and reinforced. Histologically, the specimen consisted of collagen tissue with no striated muscle. He had been well since.

CASE V.—A man, aged forty-eight years, had complained of pain in the left side of the chest for two months, aggravated by coughing, with vomiting and dyspnœa for four days. There was no definite history of trauma or any earlier relevant symptoms. He was a zoo attendant and said that he had to do heavy lifting at times. On admission to hospital, he had been a sick man, dyspnœic and distressed. There was no movement in the left side of the chest, which showed signs of pleural effusion. A chest X-ray examination had revealed an eventration of the diaphragm with mediastinal shift and a large amount of stomach in the left side of the chest. A barium bolus X-ray examination showed marked elevation of the left side of the diaphragm with paradoxical movement and volvulus of the stomach. Great relief had been obtained by gastric suction and subsequent operation revealed a three-inch rent in a thinned central portion of the left cupola of the diaphragm through which stomach, spleen and splenic colon had entered. These organs were reduced and the rent was plicated securely. Convalescence and subsequent progress had been uneventful. This appeared to be a rare case of rupture of a partial eventration on the left side.

CASE VI.—Case VI was a specimen from a baby, aged three months, who had been under Dr. Stening's care for frequent vomiting and cyanotic attacks, and who died soon after admission to hospital. The autopsy had revealed faulty development of the diaphragm on each side, so that the central portions were formed of membrane only, while the muscle arched anteriorly and posteriorly around the area of muscular deficiency. On the right side the right lobe of the liver projected into and occupied one-half of the pleural cavity. On the left side the spleen and distended stomach projected upwards similarly. None of the viscera were within the pleural sac as the membranous diaphragm enclosed them above. The lungs were malformed and collapsed and directly related to the misplaced abdominal viscera. The liver was misshapen and deeply grooved.

RUSSELL HOWARD (Melbourne) stated that he was relieved to see a post-mortem specimen amongst Dr. Goulston's series. He had had three cases, and two of the patients had died. Dr. Howard's first two patients had presented on the first day of life with gross respiratory distress. In one case the right hemidiaphragm was involved, the liver being pushed upwards to the apex of the right lung. The second case involved the left hemidiaphragm. One of these patients died in the operating theatre. Dr. Howard went on to say that these infants died of hypoplasia of the lungs which at times was associated with eventration of the diaphragm, and diaphragmatic hernia. He felt that one infant died because of severe positive pressure respiration performed in an attempt to expand the lungs. This succeeded only in damaging the normally functioning lung, having no effect on the hypoplastic areas. In Dr. Howard's third case there was an eventration of the diaphragm associated with a partial volvulus of the stomach. The infant presented with vomiting and had not been thriving. Dr. Howard felt that the optimal operative approach was through the chest because of the subsequent access to the diaphragm. He stated that at operation a diaphragm was found which was stretched—therefore stretchable material should not be used for repair. He inserted tantalum mesh between the plicated leaves of the eventrated part of the diaphragm. Satisfactory and comparatively long-term results had been reported from this procedure.

Nephritis following Infection with Individual Types of Streptococcus Pyogenes.

MARGARET C. HOLMES (Melbourne), in presenting a paper on nephritis following infection with individual types of *Streptococcus pyogenes*, said that it had been suggested in the literature by Rammelkamp, Weaver and Dingle in 1952, and Wilmers, Cunliffe and Williams in 1954, that infections with certain strains of *Streptococcus pyogenes*, notably Type 12 and a provisional type known as the Red Lake strain (Updyke, Moore and Conroy, 1955), were likely to be complicated by acute glomerulo-nephritis.

She said that since 1950 strains from forty sporadic cases of nephritis in Victoria had been typed at Fairfield Hospital, Melbourne. Type 1 had been isolated in five cases, Type 12 in eleven, provisional Type Gerrard in fourteen, and seven other types in the remaining ten cases. Provisional Type Gerrard was related to, but had not yet been proved identical with, Updyke's Red Lake strain. In 1954 an outbreak of scarlet fever had occurred in a primary school in Williamstown. Among 66 cases of scarlet fever in school children and their contacts there were 16 children who developed clinical attacks of acute nephritis. *Streptococcus pyogenes* Type 12 was isolated in fifteen cases during the outbreak.

Dr. Holmes said that since 1955, in conjunction with the Royal Children's Hospital, Melbourne, a fellow-up survey of children attending the casualty department with streptococcal sore throat had been carried out. Of 236 patients who had been followed up to date only two developed nephritis which in both instances followed a Type 1 infection. No child developed rheumatic fever. Twenty-seven patients were infected with Type 1, 22 with Type 12 and three with Type Gerrard.

In conclusion, Dr. Holmes said that it seemed in Victoria at the present time that Type 1, Type 12 and provisional Type Gerrard strains of *Streptococcus pyogenes* might have nephritogenic properties.

HELEN WALSH (Sydney), in opening the discussion, said that as far as she was aware this was the first attempt to elucidate the epidemiology of acute glomerulo-nephritis in Australia. Quite recently Rammelkamp had published yet another report of an outbreak of Type 12 streptococcal infections in a closed naval establishment. There had been 152 patients, of whom 108 were given a placebo. Of the 108 patients, 11·1% developed acute glomerulo-nephritis and an additional 15·7% had hæmaturia alone. She said that this 26% was an extraordinarily high incidence of glomerular damage, but was comparable to Dr. Holmes's figures from the Williamstown area. In her series, 25% of scarlet fever patients developed acute nephritis. Forty-four patients were treated with penicillin, and of these 4·5% developed acute glomerulo-nephritis, and an additional 7% had hæmaturia alone. This was a total of 11% with glomerular damage compared with 26% in the untreated group. These results did not show the same dramatic improvement after treatment of the streptococcal infection with penicillin as in similar studies designed to prevent rheumatic fever.

Dr. Walsh then considered what could be done to prevent acute glomerulo-nephritis, and said that first all streptococcal infections should be treated adequately. It was more generally agreed that penicillin was the "drug of choice", and as it appeared that early glomerular damage occurred in infection with nephritogenic strains, penicillin had to be given early if nephritis was to be prevented. Secondly, Dr. Walsh said that the streptococcus should be eradicated from patients already suffering from acute glomerulo-nephritis and spread of a potentially dangerous type of organism would be prevented. Thirdly, she said that when a child developed acute glomerulo-nephritis it seemed reasonable to swab the throats of close contacts, as in the family or possibly kindergarten or class groups, and so eradicate the organism by the administration of penicillin. However, swabbing of larger groups offered administrative difficulties.

Dr. Walsh went on to say that there was good evidence to show that type-specific antibodies persisted in the bloodstream for several years. After infection with, say, Type 12 streptococcus, children were immune to that type, but normally susceptible to heterologous types. In other words there was one nephritogenic strain to which these children were then immune, and they were less likely than others to contract acute glomerulo-nephritis. That fact explained the clinical observation that often after full recovery from acute glomerulo-nephritis recurrences were extremely rare. Consequently in contradistinction to rheumatic fever there was no indication for continuous prophylaxis. In conclusion, Dr. Walsh said that she would be anxiously awaiting Dr. Holmes's later results.

Dr. Holmes, in reply, said that she agreed with Dr. Walsh that penicillin was effective in preventing nephritis and quoted a series of patients reported by Rammelkamp. She said that in that series 50 children were treated with penicillin and not one developed nephritis, whereas 30 others were treated with γ globulin and six developed nephritis. She thought that those figures showed the relative merits of the two substances and considered that penicillin should be given early and in adequate dosage to children with streptococcal infections.

Calcium Disodium EDTA in the Treatment of Pink Disease.

J. E. McCOY (Melbourne) presented the results of a controlled therapeutic trial using calcium disodium EDTA in pink disease. He said that the trial had been carried out in the Clinical Research Department of the Royal Children's Hospital, Melbourne. The study consisted of ten infants, five of whom received treatment with the drug and five were used as controls.

Dr. McCoy said that since the original observations in 1948 by Swiss and American workers, many people considered mercury to be the cause of pink disease, although no unanimity of opinion existed at present. A recent advance had been the use of chelating agents in the treatment of heavy metal poisoning, and it had been suggested that pink disease might be cured in that way. With that in mind, a controlled therapeutic trial had been undertaken with the use of calcium disodium ethylene diamine tetra-acetate, a chelating agent which had been shown to bind heavy metals to form non-toxic, non-ionic complexes which were readily excreted by the kidneys.

Dr. McCoy said that the patients selected all had well-marked vascular phenomena of tachycardia, hypertension and impaired circulation of the hands and feet, and that the phenomena were uncomplicated by infection or a long history of upset in general management. The cases were divided into control and treated groups by the use of random numbers, and two independent observers had assessed progress until the children were cured.

Dr. McCoy thought that had the trial been successful, it would have provided not only an effective therapeutic measure but also evidence suggesting mercury as an ætiological agent in pink disease. Moreover, evidence of the values of the drug in mobilizing and enhancing the urinary excretion of mercury in humans could be obtained.

The results of the experiment were tabulated by Dr. McCoy and showed that the children had all been given teething powders containing calomel, and that although the average for each child was sixteen powders, the range was from two to forty-eight powders. The average age when teething powders were first given was eight and a half months and the average age at the onset of symptoms of pink disease was ten months. The mean urinary excretion of mercury in both groups on the children's admission to hospital was 44·8 microgrammes per twenty-four hours; in the treated group the excretion at that time was 53 microgrammes per twenty-four hours. Subsequent treatment with calcium disodium EDTA had failed to enhance the excretion of mercury, the mean urinary excretion after two seven-day courses being 46·6 microgrammes and 32·6 microgrammes respectively. The children treated with the trial drug were cured of the disease fifteen weeks after the onset and the control children were cured in sixteen weeks. The difference in the two groups was not significant.

Concluding, Dr. McCoy said that the experiment showed nothing conclusive on the role of mercury in pink disease. But it did show that calcium disodium EDTA had no therapeutic value, nor did it enhance the urinary excretion of mercury in pink disease.

F. W. CLEMENTS (Sydney), in opening the discussion, said that all members would compliment Dr. McCoy on the excellent way in which the experiment had been designed and would sympathize with him that he had obtained negative results. The fact that the chelating agent had proved unsuccessful in eradicating mercury had no significance in respect of the hypothesis that mercury poisoning or sensitivity was the cause of pink disease. He said that there was some experimental evidence to show that mercury was present in the body in several forms, and that it was only the inorganic and free mercury which was excreted. It would seem that more had to be learned about the biochemical process which converted mercury to the free excretable form. When this was known, it would be easier to interpret the results of experiments like those described by Dr. McCoy.

STANLEY WILLIAMS (Melbourne) said that he wished to support the implication made by Dr. McCoy that the ingestion of mercury was not the only factor in the development of pink disease. He said that it was common to obtain a history that irritability was present prior to the administration of teething powders.

R. G. DE CRESPIGNY (Adelaide) said that American pædiatricians had no doubt that the ingestion of mercury was the cause of pink disease. In Adelaide mercury had been found in considerable amounts in the urine of infants with pink disease during the period 1952 to 1954. In fact, every child with the disease admitted to the Adelaide Children's Hospital over that time had excreted mercury in the urine. In 1954 legislation had been introduced which forbade the use of mercury in teething powders, and after that not one case of pink disease was seen over a period of twelve months. However, during the past six months Dr. de Crespigny had seen two cases. The first patient was an infant who presented with typical features six weeks after recovering from a severe meningococcal septicæmia. There was no history of ingestion of mercury and no excretion of mercury in the urine. The second was a typical sufferer from pink disease of insidious onset, and again there was no history of mercury ingestion and mercury was not excreted in the urine. Dr. de Crespigny said that in his opinion that observation indicated that mercury was not the sole ætiological factor in pink disease. He thought it was interesting that the first patient developed pink disease six weeks after an assault on the adrenals.

R. SOUTHBY (Melbourne) said that he was interested to hear Dr. de Crespigny's remarks and wondered if similar observations had been made in other States. Personally, he was not convinced that mercury was solely responsible for this condition. He asked what action had been taken by the various State health departments about excluding mercury from teething powders.

P. A. EARNSHAW (Brisbane) said that during the previous twelve months he had seen only one case of pink disease.

In that instance the infant had been given forty teething powders over a period of six weeks. The powders had been stored in the house and had been purchased prior to the introduction of legislation in June, 1954, banning the sale of mercury in any form for oral administration to children under five years of age without a doctor's prescription.

CLIFTON WALKER (Sydney) asked why teething powders only were being considered, as mercury was available in many other forms such as ointments.

KATE CAMPBELL (Melbourne) mentioned the diet of the infants in question and wondered whether it played any part in the development of pink disease. Her impression was that the condition did occur more commonly in breast-fed than in artificially fed babies. She asked Dr. McCoy how many infants in his series had been breast fed. In considering the question of mercury as an ætiological factor, she thought that the disease resulted more from an abnormal reaction to mercury than from mercurial poisoning. She asked Dr. McCoy whether there was a high incidence of allergy in the infants and their relatives.

Dr. Clements said that he could answer Dr. Southby's query regarding State legislation pertaining to mercury in teething powders. He said that legislation banning mercury had first been introduced by South Australia and later by Queensland and Tasmania. Nothing as yet had been done in New South Wales and Victoria.

In replying to questions, Dr. McCoy said that the primary object of the investigation had been to determine the effect of calcium disodium EDTA on the excretion of mercury in the urine of infants with pink disease and to observe whether clinical response to treatment was altered in any way by the exhibition of that material. The part played by mercury as an ætiological factor in pink disease was only of secondary importance in this study, although it had been shown that all the infants did have a history of mercury ingestion and excreted mercury in the urine. He said that the incidence of allergic manifestations in the children and their families was no higher than that generally met with in the community. He said that in his series, nine of the ten children had been breast fed for periods ranging from two weeks to eleven months, but only three had been breast fed for longer than three months. Only one infant was still being breast fed at the time symptoms of pink disease developed. Dr. McCoy went on to say that in Victoria most teething powders did not now contain mercury, and this fact was marked on the packet in which they were dispensed. However, mercury was still procurable without difficulty as there was no legislation to prevent a chemist in his own pharmacy from dispensing mercury in teething powders. In conclusion, Dr. McCoy said that in regard to sources of mercury other than teething powders, ointments, worming powders, and napkin rinses containing biniodide had been implicated. In Melbourne a few infants had been observed who had mercurochrome or mercury ointments applied to the skin and had not developed pink disease; one child who ingested mercury ointment subsequently excreted abnormal amounts of mercury in the urine but did not develop symptoms of the disease.

The Clinical Features of Small Bowel Obstruction and of Hirschsprung's Disease in the Neonatal Period.

DAVID L. DEY (Sydney), in presenting his paper on the clinical features of small bowel obstruction and of Hirschsprung's disease in the neonatal period, said that for practical purposes colonic obstruction in the neonatal period denoted Hirschsprung's disease, if those cases due to imperforate anus were excluded. In a series of 41 cases of colonic obstruction over a seven-year period 23 were due to imperforate anus, and fifteen of the remaining eighteen to Hirschsprung's disease. The other three comprised two cases of atresia, and one of rather indefinite extrinsic origin. The classical picture of colonic obstruction was one of constipation and peripheral abdominal distension, with pain and especially vomiting as later and less urgent features. The symptoms and signs of neonatal Hirschsprung's disease in this series were found to conform largely with this concept, with the one exception that vomiting was an early and constant feature. Distension was noted in every case, but on the first day in only three instances, the remainder being recognized on the second day, with two on the third day. Constipation was also present in every case (except one in which there was gross watery diarrhœa), but was by no means absolute or even constant. The vomiting, he said, was apparent in every case, and in all but two preceded the distension or was coincident with it. In one of the two it did not appear for three weeks, but distension was noted on the second day; in the other it followed hard upon the distension. In three cases only did bile appear in the vomitus, in two of the three the appearance of bile was intermittent, and in no case was the vomiting described as progressive. Two of the babies were premature, three showed other abnormalities, and two had perforation of the colon with pneumoperitoneum. There was a gross male preponderance of 14:1.

Dr. Dey said that small bowel obstruction in the neonate was more frequent, there being in the same seven-year period 15 cases of duodenal obstruction, 17 cases of *volvulus neonatorum*, and 32 of obstruction of the small bowel. There were in addition four cases of neurogenic paralysis, three of obstruction from hernia, ten of meconium ileus and five of meconium peritonitis. With the exception of the groups associated with meconium ileus and meconium peritonitis, all the babies in whom the obstruction lay below the duodenal papilla presented similar clinical features, but with varying degrees of distension. Occasionally some special finding (such as melæna in *volvulus neonatorum*) proved helpful in diagnosis.

Dr. Dey said that the classical concept of the picture of small bowel obstruction was one of pain and shock, of progressive bilious vomiting, with distension and constipation as later and often less urgent components. In the neonate pain did not appear to be a striking feature, although the infant might be restless and uncomfortable. "Shock" as opposed to "dehydration" had not appeared to be of much significance, and when present was likely to denote a vascular accident, such as mesenteric thrombosis (two cases) or a tight volvulus. The vomiting was that part of the picture which was most worthy of consideration. It was noteworthy that even in cases of complete atresia of the jejunum the onset of vomiting might be delayed for as long as four days. Presumably during this period little fluid had been ingested, but in any case it appeared likely that the alimentary secretion was often at a low level in the first few days of life. Physiology text-books were silent on that point. Symptoms usually began soon after birth with vomiting which as a rule occurred after feeds only. However, the vomiting increased very rapidly in quantity and frequency, and in the vast majority of cases in which the obstruction lay below the duodenal papilla the vomitus soon became bile-stained. Fæcal vomiting followed in the absence of relief. In the early stages the volume of the vomitus appeared of first importance from the diagnostic point of view. Even when no bile was present, if a baby had copious vomiting after having previously emptied his stomach after a feed, he should be regarded as probably suffering from obstruction and investigated accordingly. Constipation was often absolute, at the most a little mucus only being passed. However, particularly in those cases in which the obstruction was high in the small bowel, one or even two small meconium stools might be observed. Distension was noted as being present in about two-thirds of the cases. The onset was not clearly stated in most of the case notes, but appeared to follow the onset of vomiting. It was central and was often found mainly in the upper part of the abdomen. Visible peristalsis might be observed in an appreciable number of cases.

Dr. Dey presented two clinical pictures. In one a male child in the first day or two of life began to vomit. The vomiting was not unduly severe and was perhaps intermittent, but the vomitus on rare occasions contained bile. Shortly after this the child's abdomen was found to be distended, and on inquiry it would be found that he had passed meconium on one or two occasions only. Such a patient was likely to suffer from Hirschsprung's disease, and the diagnosis might be clarified by the passage of a rectal tube, by a plain X-ray examination of the abdomen, or in some instances by barium enema. The other clinical picture was of an infant who began to vomit similarly in the first day or two of life. However, in such an instance the vomiting was progressive and soon became copious and independent of meals, the vomitus was stained with bile, and eventually became fæculent. Distension was central and progressive, visible peristalsis might be present, and virtually complete constipation might occur. Such a child had a small bowel obstruction, which could usually be verified by a plain X-ray examination of the abdomen—and in Dr. Dey's view needed early surgical relief.

In conclusion, Dr. Dey said that if a baby was born with abdominal distension already present, or if distension was noted in the first few hours, the baby was likely to be suffering from meconium ileus (in which case the loaded coils of bowel might be felt) or meconium peritonitis (with signs of intraperitoneal gas, or fluid, or both).

RUSSELL HOWARD (Melbourne), in opening the discussion, stated that if the obstruction was complete, and most organic

obstructions were complete or almost complete, the diagnosis was usually obvious. These infants presented with vomiting on the first day of life; the vomitus became rapidly bile stained and later fæculent. Such a case was not one of Hirschsprung's disease and it was imperative to operate early. Dr. Howard stressed the need for urgent operation in the presence of abdominal distension. He further stated that the diagnosis of Hirschsprung's disease was often not apparent early, vomiting was often not an early feature, and often did not occur until the end of the first week or later. Hirschsprung's disease behaved as a subacute obstruction, often of the intermittent type, and there might be periods when bowel actions were occurring. These infants might not be recognized until the second or third week. In regard to X-ray diagnosis, Dr. Howard was sure that it was impossible to distinguish small from large bowel radiologically in the newborn period. If the X-ray film showed universal distension of bowel, the diagnosis was almost invariably Hirschsprung's disease. Rarely it might indicate a very low intestinal obstruction. A barium enema, he said, was of no help in the diagnosis of Hirschsprung's disease before the third to fifth week. He said finally that if the finger could be passed above the recto-sigmoid junction in an infant and this procedure was followed by the evacuation of a large amount of fæces, a diagnosis of Hirschsprung's disease was almost invariable.

E. STUCKEY (Sydney) stated that the early picture of small bowel obstruction in infancy was one of vomiting without abdominal distension. He thought that the patients came to operation late (third to fourth day) when the presence of copious vomiting, even in the absence of feeding on the first and second days, should suggest the diagnosis. The diagnosis, if suspected, was easily confirmed by X-ray examination of the abdomen. He agreed with Dr. Dey that Hirschsprung's disease often presented early with vomiting. He also agreed with Dr. Howard that a rectal examination producing a large amount of meconium was a valuable means of diagnosing Hirschsprung's disease. Distension also helped in the diagnosis—it was a universal distension. If this universal distension was shown radiologically and there was air in the rectum, Dr. Stuckey stated that a diagnosis of Hirschsprung's disease was very likely. A visible ladder pattern on the abdomen, too, was helpful, but it took about two weeks to develop.

CLIFTON WALKER (Sydney) cited cases of atresia of the terminal part of the ileum and had been impressed with the large amounts of meconium passed by these infants. He asked Dr. Dey where this meconium was formed.

M. SOFER SCHREIBER (Sydney) commented on the reason why an infant with a complete intestinal atresia might nevertheless pass bile-stained meconium stools. He pointed out that the recent experimental work of Louw, of Capetown, had established that intestinal atresia was due to an intrauterine thrombosis of the blood vessels supplying the affected portion of fœtal gut, and not to the persistence of epithelial concrescences as usually believed. Hence the bile had passed downwards through the patent normally formed gut into the colon before the vascular disturbance causing the atresia had occurred. Regarding the sign of abdominal distension, he recalled an infant whose abdomen had been grossly distended at birth, necessitating episiotomy for delivery of the abdomen. This child had an intestinal atresia. After operation the abdomen remained distended, and at a second operation some days later a second more distal atresia was found, resection of which was followed by recovery.

In reply to Dr. Clifton Walker, Dr. Dey stated that in the cases under discussion there was quite a profuse secretion of mucus, epithelial elements *et cetera* by the colonic wall, and that the meconium seen in cases of ileal atresia was formed in the colon. In his experience Hirschsprung's disease presented a more acute picture than had been presented by Dr. Howard, and he had found it important to consider its distinction from small bowel obstruction.

Correspondence.

THE MEDICAL BENEFITS FUND OF AUSTRALIA AND SERVICES RENDERED IN PUBLIC WARDS OF HOSPITALS.

SIR: Dr. H. R. R. Grieve's letter in THE MEDICAL JOURNAL OF AUSTRALIA of July 14 brings to mind several problems, which are long overdue for some explanation, both by the Council of the British Medical Association and the Executive Committee of the Medical Benefits Fund.

Firstly, whilst Commonwealth benefit is not payable for services rendered in public wards, what barrier exists to prevent payment of fund benefit in these cases? Recently, I had experience of a patient who had consulted an ophthalmologist for purposes of refraction. Commonwealth benefit is specifically mentioned as being not payable when a patient has consulted an eye specialist for refraction. However, in this instance the fund made an ex-gratia payment of fund benefit. If Dr. Grieve is sincere in his letter, which I take him to be, why then does the fund not make ex-gratia payments of fund benefit to public ward patients?

Secondly, for the past year, patients classified public, after making a claim on the Medical Benefits Fund, have received a stereotyped letter which infers in no uncertain manner that the doctor who sends an account to a public ward patient is guilty of a heinous criminal offence. Why has not some action been taken by the British Medical Association at least to amend the wording of this letter, which is an example of the worst type of sabotage the good name of the medical profession has to bear?

Thirdly, just what action has been, and is being, taken by the Council of the British Medical Association to have amended the law relating to the charging of public ward patients? If statements on this matter were made in the journal at regular intervals, it would reassure the country practitioner that tangible efforts to change this iniquitous law are being made. So, now is as good a time as ever for the first statement: Are serious steps being taken; if so, what are they—or is it a matter of comparative disinterest to most members of the Council, who, being mainly city practitioners, are little if at all affected?

Yours, etc.,

Town Hall Building,
Otho Street,
Inverell,
New South Wales,
July 17, 1956.

G. A. SCARLETT.

SIR: In my previous letter I stated: "In its administration the Medical Benefits Fund is strictly bound by the terms of the *National Health Act* in this and other related matters." It would have been well had that general statement been fully accepted by Dr. Scarlett. He should realize that all medical benefit organizations—not the Medical Benefits Fund alone—have little or no choice where the payment of government benefits is concerned.

In the particular matter raised in Dr. Scarlett's first paragraph, all registered medical benefit organizations in New South Wales are expressly forbidden, in terms of the circular N.M.13 issued by the Commonwealth Deputy Director of Health in New South Wales in view of the provisions of Section 36 of the New South Wales *Public Hospitals Act*, from paying any benefit for services rendered to a patient classified as public. This instruction by the Commonwealth must, of course, be obeyed, and it is not sabotage to obey the law.

Further, in the type of case mentioned by him, the Medical Benefits Fund pays its own benefit for an ophthalmological service, not *ex gratia*, but as a matter of moral and legal obligation to the contributor, because in this case the contributor pays a fee. In the case of the patient classified public, the contributor pays no fee, and payment of a fund benefit would therefore also be forbidden by the 90% rule.

The circular letter referred to in Dr. Scarlett's third paragraph was drafted by the claims officers of the fund in accordance with the above-mentioned Commonwealth circular. The words of this letter were altered about one month ago in accordance with the Executive Committee's wishes. It is hoped the new form will be approved.

Finally, it is unfortunate that Dr. Scarlett, even in ignorance of the true position, should write anything to perpetuate the illusion, sedulously fostered by political critics, that the Medical Benefits Fund is in any degree under the control of the British Medical Association. The Medical Benefits Fund, though formed by a decision of the

British Medical Association Council (New South Wales Branch), has never been in any degree or in any way under the control of that body.

Yours, etc.,

"Caberfeidh",
113 Homer Street,
Undercliffe,
New South Wales.
August 8, 1956.

H. R. R. GRIEVE,
Chairman, Medical Benefits Fund.

SIR: Dr. G. A. Scarlett in his letter of July 17, 1956, asks what action has the Council of the British Medical Association (that is, New South Wales Branch) taken to have amended the law relating to the charging of patients classified as public patients.

The answer to this question is that the Council has made frequent representations to the Government to permit of public patients, who are insured with medical benefit organizations, being charged by their medical attendants.

Whilst the State Minister for Health expressed sympathy with the Council's representations, he pointed out that the Commonwealth Government laid down as a condition that the total benefit paid must not exceed 90% of the doctor's charge. This would in effect mean that the contributor patient must be directly responsible for at least 10% of the charge, and this was unacceptable to the State Government in so far as it related to public patients.

Having regard to the basis on which rates of contribution to the Medical Benefits Fund were determined, that is, that every contributor to the fund would be entitled to benefits, the Council is firmly of the opinion that payment of benefits should be made in all cases of insured persons in public hospitals, irrespective of their classification.

Dr. Scarlett can rest assured that the question of classification of patients and the application of a proper means test is receiving the full consideration of the Council. In the next monthly notice every member will receive a copy of the hospital policy of the Branch.

Finally, the Council is in no way responsible for the stereotyped letter sent by the Medical Benefits Fund to contributor patients.

Yours, etc.,

EDGAR THOMSON,
President.

British Medical Association (New South Wales Branch),
British Medical Association House,
135 Macquarie Street,
Sydney.
August 8, 1956.

Notice.

VICTORIAN BRANCH NEWS.

THE next meeting of the Section of Industrial Medicine of the Victorian Branch of the British Medical Association will take the form of a plant inspection of the Fairfield mill of the Australian Paper Manufacturers, Limited, on Tuesday, August 21, 1956, at 8.30 p.m. The mill is situated at 626 Heidelberg Road, Alphington, and plant operation and medical facilities will be demonstrated by Dr. L. R. Minogue. All members of the Branch are invited to this inspection.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

King, Errol Edward Trevor, M.B., B.S., 1945 (Univ. Sydney), Cliftonville Road, Maroota, via Windsor, New South Wales.

Finlayson, Jean Stanley, M.B., B.S., 1939 (Univ. Melbourne), Smart Street, Charlestown, New South Wales.

Lang, Francis Houstoun, M.B., B.S., 1955 (Univ. Sydney), 15 McIntosh Street, Gordon, New South Wales.

The undermentioned has applied for election as a member of the South Australian Branch of the British Medical Association:

Carter, Melville Lionel, M.B., B.S., 1952 (Univ. Adelaide), 14 Greenhill Road, Glenside, South Australia.

The undermentioned have been elected as members of the South Australian Branch of the British Medical Association: Cooke, Theodore John Lloyd, M.B., B.S., 1956 (Univ. Adelaide); Forbes, David Stewart, M.B., B.S., 1955 (Univ. Adelaide); Robertson, Anthony Oliver, M.B., B.S., 1956 (Univ. Adelaide); Cox, John Samuel Tweedale, M.B., B.S., 1955 (Univ. Adelaide); Appleby, Robert William, M.B., B.S., 1956 (Univ. Adelaide); McLeay, Colin James, M.B., B.S., 1956 (Univ. Adelaide).

Deaths.

THE following deaths have been announced:

BIRNIE.—Robert Kenneth Birnie, on August 6, 1956, at Glen Iris, Victoria.

TRATHEN.—James Elvins Trathen, on August 6, 1956, at Buxton, Victoria.

Diary for the Month.

AUG. 21.—New South Wales Branch, B.M.A.: Medical Politics Committee.
AUG. 22.—Victorian Branch, B.M.A.: Branch Council.
AUG. 23.—New South Wales Branch, B.M.A.: Clinical Meeting.
AUG. 24.—Queensland Branch, B.M.A.: Local Association Conference.
AUG. 24.—Queensland Branch, B.M.A.: Bancroft Oration.
AUG. 25.—Queensland Branch, B.M.A.: Annual General Meeting.
AUG. 27.—Victorian Branch, B.M.A.: Branch Meeting.
AUG. 28.—New South Wales Branch, B.M.A.: Ethics Committee.
AUG. 30.—New South Wales Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

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All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

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